LEPROSY IN INDIA

A Quarterly Record of the Study of Leprosy
and of Anti-leprosy Work
in India and in other Countries

CONTENTS:

NOTICE

Contributions for *Leprosy in India* should be addressed to the Leprosy Research Laboratory, School of Tropical Medicine, Calcutta. Contributions need not necessarily be purely scientific but may deal with any topic of general interest in the campaign against leprosy. Contributions should preferably be typed in duplicate; if written, one side only of the paper should be used. Contributions for the next number should be submitted before the 15th of March, 1944

Leprosy in India is obtainable from the Hony. Secretary, British Empire Leprosy Relief Association (Indian Council), New Delhi. The subscription rate is Indian Rs. 2/- and foreign Rs. 2/8/- including postage. Single copies As. -/8/- including postage.

Instruction course in leprosy

The special course in leprosy under the auspices of the Indian Council of the British Empire Leprosy Relief Association which was announced in the October 1943 issue of this journal had to be postponed because sufficient number of candidates did not offer for the course It is now proposed to hold the course from the 17th to the 29th of April, 1944, provided sufficient number of candidates are forthcoming Applications for admission to the course should be sent to the Officer-in-Charge, Leprosy Research Department, School of Tropical Medicine, Calcutta to reach him before the 15th of March, 1944

ORIGINAL ARTICLES

AN INTRODUCTION TO THE STUDY OF THE INCIDENCE OF LEPROSY IN WEST CHINA

By WALLACE CRAWFORD *The Leper Hospital of the College of Medicine and Dentistry West China Union University Chengtu Szechwan*

The incidence of leprosy in West China

This paper is just what its name implies, namely an introduction to the study of the incidence of leprosy in West China, for there never has been any study into the incidence of the disease in these parts Two partial attempts have been made, one by Dr James L Maxwell the well known leprologist now retired and the other by the author of this paper

In 1935 Maxwell made a short trip into West China where he made a short study of the incidence in one part namely the borders of the provinces of Szechwan Yunan and Kweichow and his findings showed that the incidence of the disease in those parts was as high as anywhere else in China. In his book Leprosy while discussing the distribution of the disease Maxwell[1] states that in the western provinces (Western Yunan, Western Szechwan (Sikang) Kansu and Eastern Tibet) the incidence of the disease is very great, over 1 per 1 000 i.e. similar to that in Kwangtung

In 1934 in collaboration with Dr Maxwell the writer sent out thirty large-scale maps of the province of Szechwan to as many missionaries living in the various parts of the province, mostly on its periphery asking each to record on the map the cases of leprosy which came to his attention, marking on the map the location of the cases and if possible, giving some short details of it, particularly regarding origin residence, etc. At the end of the year we had the maps collected and the information correlated. We found that there were some five areas in which the disease is endemic and from which we since have had cases come to the hospital. Other endemic centres have later come to light since the opening of the leper hospital in Chengtu, under the West China Union University College of Medicine and Dentistry

Apart from the two investigations mentioned above, we have little or no information regarding the incidence of leprosy in these parts of West China. However Dr Pearce[2] of the China Inland Mission, Kaolan (Lanchow) published an article in 1939 in which he gives considerable details regarding the places from which the leprosy patients came to the hospital at Kaolan This information is restricted almost entirely to the provinces of Kansu and Ch in Hai

During the summer of 1941 the writer was one of a survey party into the provinces of Shensi Kansu and Ch in Hai when he was able to corroborate the findings of Pearce and also to locate several other endemic centres.*

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*The author had included details of these centres in his article These details as also the sketch maps have been omitted from the published article, since they are only of local interest.—ED *Lep in India*

TREATMENT OF LEPROSY COMPLICATED BY SYPHILIS

By D N Bose, *Medical Officer, Asansol Leper Hospital and Settlement*

Introduction

Leprosy is a chronic disease It may be associated with any other infection which would devitalise the patient, help in the aggravation of the parent disease (leprosy), and thus retard the progress of the patient Hence the general principles in the treatment of leprosy have been to eliminate, first of all, the complicating diseases

Syphilis is one of the commonest co-existing maladies in leprosy cases, specially in an industrial area like Asansol Mining Settlement where about 16 to 20% of leprosy cases registered for treatment show a positive Kahn reaction with or without any history or clinical evidence of syphilis So it has been our routine practice to do Kahn test on all the leprosy cases on admission for treatment at the leprosy clinics

To treat so many syphilitic cases, who are mostly poor and who come from labour class, with arsenical preparations like N A B , neo-salvarsan, solu-salvarsan, sulf-arsenol, etc., is a huge economic problem Arsenic is suitable for rich patients, or for hospital patients who take injections at the cost of the State In a leprosy clinic where the average attendance of patients per clinic day is 160 to 180 of whom about 30 are syphilitic, where treatment is to be offered within specified hours, and where funds are limited, some cheaper remedies to combat both the maladies (syphilis and leprosy) together should be thought of

Avenyl (B W & Co), a mercury preparation though not very cheap, dissolved in hydnocarpus oil or its esters, was advocated for the purpose, and was long in use, but the results were found discouraging and hence its use has now been discontinued

The use of bismuth against *Treponema pallidum* has been advocated by many eminent authorities for a long time. The chemotherapeutic effects of bismuth are considered to be specially marked in late manifestations of syphilis Bismuth, unlike other specific remedies, has a sustained parasiticidal action after being acted on by the tissues

Therefore the possibility of successfully treating cases of leprosy complicated with syphilis with a combination of bismuth and hydnocarpus oil was investigated The results obtained with this method of treatment have been encouraging and are reported below

Combined treatment with bismuth and hydnocarpus oil

The preparation used—Bismuth Salicylate or Bismuth Oxy Salicylate (Howards'), a whitish amorphous powder insoluble in water and alcohol, is fairly cheap (Re 1 per ounce at pre-war rate) A 3% suspension of this powder in 4% creosoted hydnocarpus oil or its esters is made in a sterile pestle with a mortar When bismuth and oil are thoroughly mixed, the mixture is poured into a clean stoppered phial and sterilised in oil-bath at a temperature of 130° centigrade for half an hour If the mixture is kept for some time, bismuth may be deposited at the bottom of the phial, but this does no harm, at the time of giving injection the phial should be well shaken and the powder re-suspended

	Age	Sex.	Type and stage of leprosy	History of syphilis or any clinical evidence of syphilis when admitted.	Kahn s reaction on admission.	Total quantity of mixture injected with quantity of Bismuth salicylate	Kahn s reaction after injection.	Progress in leprous lesions after injection.	Remarks.
1	12	M	N1	nil	4+	88 c.c. with 41 grs. of bismuth.	Neg	Definite improvement noticed. Patch almost subsided	Discontinued treatment.
2	20	F	N2	nil	4+	130 c.c. with 60 grs. of bismuth.	Neg	Patches thinner Some of them subsided.	Continuing treatment.
3	28	M	N2	nil	2+	20 c.c. with 9 grs. of bismuth	Neg	Patches subsided Permanent damages persisting	Do
4	33	M	L. N2	nil	4+	116 c.c. with 54 grs of bismuth.	Neg	Definite changes in the physical characters of the lesions and also less number of bacilli	Do
5	8	M	N1	nil	3+	108 c.c. with 40 grs. of bismuth.	Neg	Appreciable improvement during the course of injections.	Discontinued treatment.
6	40	M	N2	History present	3+	100 c.c. with 48 grs. of bismuth.	Neg	Some of the lesions have completely subsided Other lesions much diminished	Continuing treatment.
7	40	M	N1	Do	3+	86 c.c. with 40 grs of bismuth	1+	Patch almost subsided	Discontinued. treatment.
8	50	F	L2 N2	nil	4+	94 c.c. with 44 grs. of bismuth	1+	Definite changes in the character of the lesions and also less number of bacilli	Do
9	6	M	N1	nil	3+	50 c.c. with 23 grs. of bismuth.	Neg	Patches diminished.	Do
10	25	M	L2 N2	nil	2+	28 c.c. with 12 grs. of bismuth.	Neg	Lesions thinner and diminishing Less number of bacilli.	Do
11	24	M	L2 N2	History present	4+	51 c.c. with 24 grs of bismuth.	2+	Infiltrations much thinner and subsiding	Do
12	34	M	L3	Do	4+	55 c.c. with 25 grs. of bismuth.	Neg	Nodular infiltrations have subsided. Less number of bacilli.	Do

The mode of injection —This mixture of bismuth and oil is injected intramuscularly Subcutaneous and intradermal methods are deprecated as they are likely to cause inflammation and necrosis at the sites of injections

The technique of the injection is simple, only careful insertion of a needle will prevent the damage to a vessel and thus will avert a fatal embolism The needle should be free from bismuth to avoid local irritation Gluteal region is generally the site selected for injection Draw a line between anterior superior iliac spine and inter-gluteal crease, with the middle of the line as centre describe a circle of 3 cm diameter, make all injections within this circle to avoid blood embolism and injury to the sciatic nerve, seal the site of injection with Tr Benzoin Co

Dose —The initial dose for an adult is ½ c c increased by ½ c.c every week till a maximum of 4 c.c is reached Injections are given once a week

Course —The course of the injections varies according to the nature of the syphilitic infection as determined by the Kahn test My experience has shown that a maximum course of about 4 grammes (60 grs) would make a case free from spirochetal infection, showing at the same time marked improvement in leprous lesions

Results —The results obtained with this method of treatment in 12 cases are shown in the table on p 7

Conclusions

It is considered that the combined treatment with bismuth and hydnocarpus oil is worth a trial in cases of leprosy complicated with syphilis This conclusion is based on the following considerations —

1 It is an economical cure with the least possible trouble to the patients so that they may undergo treatment without any interference in their daily routine work The toxicity of the preparation is low and the patients do not experience any inconvenience
2 The method of injection is simple and the injection can be given even by trained assistants
3 The patients can come to the doctor without any preliminary preparations which are required in the treatment by arsenical preparation.
4 The preparation of the mixture is simple and it can be easily made in the clinics
5 Arsenical intolerance in leprosy patients is fairly high and can be easily avoided by this method of treatment.
6 The results are encouraging to a great extent

[Of the 12 cases reported in this paper in none was there any clinical signs of syphilis, and in only 4 was there a history of syphilis A positive Kahn test in a case of leprosy has been considered by the author to indicate the presence of syphilitic infection We know that at least in the lepromatous cases, a positive Kahn or Wassermann test does not necessarily mean the presence of syphilis, a positive test may be caused by the leprous infection alone Sera from a large proportion of lepromatous cases are known to possess the power of fixing complement in the presence of various antigens This power of fixing complement is possessed to a less extent by the sera of the bacteriologically positive neural cases

The fact that treatment with hydnocarpus oil and Bismuth changed a positive Kahn test into a negative Kahn test cannot also be taken to mean that the patients were actually suffering from syphilis since it is known that patients with a lepromatous type of leprosy and with a positive Kahn test may become Kahn negative after treatment with hydnocarpus oil alone.—ED *Lep in India*]

TREATMENT OF THE NEURAL SYMPTOMS IN LEPROSY

By V P ALEXANDER, *Medical Officer, Leprosy Hospital, Miraj, S M C*

As we visit our patients in the leprosy institutions the most common complaints we daily hear are the sensations of burning and pin-pricks in the extremities, and pain along the main nerve trunks These symptoms are specially noted in the neural type Some cases suffer from such symptoms for weeks together, and others for months in varying degree of severity I have found the following methods of treatment quite satisfactory

1 *Wheatgerm flour (Bemax)*

Dose 1 to 2 oz daily given by mouth The drug has to be given for months together Its action is supposed to be due to its vitamin B content We have supplemented this treatment by the oral administration of 1 to 3 oz of ground-nuts daily Ninety patients with similar complaints were divided into two equal groups. One group received wheatgerm flour and ground-nuts, while the other group did not After six to eight months' observation it was noticed that the nerve pain and burning sensation in the group which received the above two articles of food were appreciably diminished

Wheat forms the major part of the diet of all our patients and during the period of our investigation with wheatgerm flour and ground-nuts all the patients continued to receive their routine treatment of leprosy with hydnocarpus oil

It was noticed that the addition of wheatgerm flour and ground-nuts did not only relieve the nerve symptoms but also improved the general health of the patients We, therefore, later started to give these two articles to all our inmates With the introduction of wheat-germ flour and ground-nuts we were able to save three-fourths of the money spent on aspirin, phenacetin and salicylates I will therefore suggest to workers in other leprosy institutions to include, if possible, these articles of food in the diet of the patients and thereby to minimise the use of analgesic drugs Dr Cochrane and his co-workers have already pointed out the importance of wheat diet in the treatment of neural complications of leprosy

2 *Magnesium sulphate injections*

Magnesium sulphate is used as a 25% solution The solution must be well sterilised The injection may be given into the nerve sheath in which case 1 to 2 c c of the solution will be sufficient If the injection is given around the nerve 2 to 5 c.c or even more may be required The injection of magnesium sulphate solution relieves the pain and burning sensation distal to the point of injection For example if the ulnar nerve is injected above the elbow, the pain and burning sensation of the fore-arm and hand in the supply of the ulnar nerve disappear almost immediately The relief, though temporary, lasts longer than that following injections of alcohol or novocaine On the average, one injection of magnesium sulphate relieves the symptoms of neuritis for two to four weeks However, I have noticed in many cases that the effect of a single injection has lasted for two to three months, and that the symptoms, when they recur, are less severe

In some cases the neural symptoms appear only occasionally and in such cases a single injection of magnesium sulphate gives great relief In such cases all other measures to relieve the symptoms such as the administration of salicylates, aspirin phenacetin or injection of alcohol or novocaine found only a second place

The nerves most commonly injected are the ulnars and the common peroneals. In a few cases the brachial plexus the sciatic nerve and the intercostal nerves were injected with good results

This treatment is contra indicated in acute inflammations of the nerve, and when the presence of nerve abscess is suspected. In case of a nerve abscess it must be opened and drained The process of stretching the nerve or removing the nerve sheath are useful in selected cases.

3 *Sodium bicarbonate injections*

1 drm. of sodium bicarbonate dissolved in 500 c.c. of sterilised saline given intravenously is specially useful in the treatment of neuritis due to lepra reaction. This method of treatment reduces the duration of lepra reaction considerably It has also been found useful in cases of neuritis apart from the reaction cases It is important that the sodium bicarbonate solution should not be heated under any circumstances. Sodium bicarbonate for intravenous injection can be obtained from the Bengal Immunity Co or can be prepared in the institution by using sterile paper and spatula for weighing

Summary

1 The addition of wheatgerm flour and ground nuts and similar articles of food which contain vitamin B to the daily diet of leprosy patients is very useful in relieving the neural complications and in improving the general health of the patients.

2 The sensation of burning and pin pricks is relieved by an injection of 25% solution of magnesium sulphate around the nerve supplying the area. The relief in many cases is temporary but the effect of magnesium sulphate has been found to last longer than that of the injections of alcohol novocaine etc

3 Intravenous injections of sodium bicarbonate have been found specially useful in the treatment of neuritis accompanying lepra reaction.

4 Magnesium sulphate and sodium bicarbonate are much cheaper than the other drugs used for relieving the nervous symptoms and therefore the extensive use of these two drugs is advocated specially in these days when the cost of drugs due to war conditions has increased very much.

REPRINTED ARTICLES

LEPROSY—THE CORRELATION OF ITS CLINICAL, PATHOLOGIC, IMMUNOLOGIC AND BACTERIOLOGIC ASPECTS

By V PARDO-CASTELLO, M D , *and* FRANCISCO R TIANT, M D., *Havana, Cuba*

[*Reprinted from the Journal of the American Medical Association*, 1943, 121, 1264]

Leprosy affects the skin, the peripheral nervous system and the mucous membrane of the nose by preference, but other tissues and organs are also affected, often early in the disease, such as the testicles, the mammary glands, the lymphatic glands, the larynx, and the eyes Late manifestations of the liver spleen and other internal organs may occur

Lesions of the muscles, bones, skin, hair, nails and mucous membranes may not be directly due to the presence of Mycobacterium leprae but to trophic disturbances caused by nerve involvement

The preference of leprosy for the skin and peripheral nerves led to the classic conception of 'cutaneous', 'neural' and 'mixed' types of leprosy However, it is evident that the great majority of patients with leprosy present symptoms and signs of cutaneous, neural and visceral involvement and therefore most cases of leprosy would fall under the heading of 'mixed leprosy

On the other hand, the fact that the clinical manifestations of leprosy affect the skin, the peripheral nervous system and many other tissues and organs does not offer a definite foundation for the classification of the types of leprosy, especially as to their prognosis, epidemiology pathology and immunology Cutaneous lesions may be severe and of bad prognosis or may be slight and of good prognosis Nerve involvement may be slight and chronic without much loss of function or may be severe, leading to rapid wasting and complete disability

The leprosy congresses of Manila in 1931 and of Cairo in 1938 considered the classification of the clinical forms of leprosy, adhering to the old ideas and preserving the cutaneous, neural and mixed types However, the South American dermatologists insist on the advisability of using a pathologic foundation for the classification of leprosy, following the suggestion made as early as 1936 by Edurado Rabello Jr of Rio de Janeiro This classification has been adopted by the South American dermatologists among whom the contributions of the Rabellos, Schujman N V Greco, Souza Lima, Moura Costa, Aguiar Pupo and Balina and Bassombrio are prominent

The pathologic changes found in leprosy are sufficiently definite and characteristic, corresponding with clearcut clinical aspects in the great majority of cases and with definite immunologic reactions and bacteriologic findings, making the correlation of these factors most important from the points of view of the prognosis and the sanitary control of the disease

Whether leprosy affects the skin , the nervous system, or the other tissues and organs, the pathologic changes may be grouped in three categories—lepromatous, tuberculoid, and simple inflammatory which we shall call non-specific To the trained eye these pathologic changes have clinical equivalents the lepromatous, represented by the nodular

infiltrative lesions, the tuberculoid represented by flat infiltrated annular or ringlike small nodular lesions and the non-specific, represented by the macular manifestations of the skin and the simple dystrophic neural manifestations.

The fact that lepromatous lesions are extremely rich in Hansen bacilli while the tuberculoid and non specific are paucibacillary and that the immunologic lepromin tests are negative in lepromatous and positive in tuberculoid types, adds strength to the practical importance of this classification.

The lepromatous and tuberculoid types are therefore definite clinical pathologic, bacteriologic and immunologic forms of leprosy The non-specific types represent transitional stages and these cases may remain non specific for a long time or may develop into lepromatous cases or into tuberculoid cases. The tissues show only perivascular inflammation with lymphocytic infiltration In some cases a few bacilli are scattered in the tissues or are demonstrable in the lymph and mucous membranes while in others few or rare bacilli are found. In 40 to 60% of these non-specific types the lepromin test is positive, while in the other 40 to 60% the lepromin test is negative. Therefore the non-specific types may progress to the severe lepromatous manifestations or slowly develop the more benign tuberculoid symptoms.

The accompanying table resumes the South American classification of leprosy modified by us to make the clinical aspects more prominent and adding the lazarine type of tuberculoid leprosy

The Lepromatous Types

When Mycobacterium leprae invades the skin mucous membranes peripheral nerves and other tissues and organs finding little or no defensive reaction the histologic features are those of a chronic infiltrating granuloma affecting the totality of the tissue. The cells are large histiocytes with special characteristics some are vacuolated and badly stained and some are huge cells filled with mucous degenerated protoplasm and innumerable accumulations of acid fast bacilli. The connective and elastic tissue disappear entirely and are supplanted by the cellular infiltrate The glands and hair follicles are gradually choked and finally atrophy

These infiltrations appear clinically as nodular formations more or less lobulated usually dark red well defined from the adjacent parts and varying in diameter from a few millimetres to several centimetres. Others are diffuse infiltrations without definite outline, more or less flat and geographic in outline. In the peripheral nerves the infiltrations may be total thickening the nerves to three or more times their normal size or may be moniliform like the beads of a large rosary along the trunk of the nerve In other tissues such as the testicle and mammary gland the lepromas affect the form of hard nodules absolutely painless and without apparent signs of inflammation. In the larynx, nose and other mucous membranes the lesions ulcerate early and deformities and mutilations are extreme. In advanced cases lesions of the liver and other internal organs present the same diffuse lepromatous infiltrations or localised nodular formations.

This is the easiest type to diagnose and the cutaneous lesions may be recognised even by the layman in countries where leprosy is common.

Pathology			Immunology (Lepromin test)	Bacteriology
Leprosy of the skin	Lepromatous		Negative	Numerous bacilli
	Tuberculoid	Miliary	Positive	Rare bacilli
		Sarcoidal	Positive	Rare bacilli
		Lazarine	Positive	Abundant bacilli in necrotic areas rare in tissues
	Non specific	Erythematous	Pos or Neg 50%	Few bacilli
		Pigmented	Pos or Neg 50%	Few bacilli
		Achromic	Pos or Neg 50%	Few bacilli
Leprosy of the nerves	Lepromatous		Negative	Numerous bacilli
	Tuberculoid	Miliary / Colliquative	Positive	Rare bacilli
	Non specific		Pos or Neg 50%	Few bacilli
Leprosy of other tissues and organs	Lepromatous		Negative	Numerous bacilli
	Tuberculoid	Miliary / Sarcoidal	Positive	Rare bacilli
	Non specific		?	?

Bacteriologically the lepromatous lesions are so full of acid fast bacilli that in the tissues they may be seen with the small dry objective in the form of bright red patches spread throughout the microscopic field. Two methods may be employed to examine tissue for bacteriologic diagnosis one may remove a piece of a leproma by means of a small curved scissors imprinting the tissue juices on several cover slides or make a small incision in the mass of the leproma scraping off the soft tissues in the bottom of the wound with the scalpel and spreading the juice thus obtained on a cover slide. When proper staining is done by the Ziehl Neelsen method the number of acid fast bacilli in these preparations is enormous It must be remarked that the specimens obtained from the mucous membrane of the nose should be taken by scraping the mucosa as deeply as possible without causing hemorrhage.

Immunologically lepromatous types show absolutely no reaction when tested with lepromin. Sometimes an early non-specific reaction appears after the first or second day but disappears without leaving any trace. This absence of allergic response to lepromin means that the patient offers no defense to the infection. Therefore the prognosis of these cases is bad.

From a prophylactic point of view lepromatous cases are dangerous being open and literally oozing Mycobacterium leprae of the highest virulence. These are the cases that must be isolated from the community

The Tuberculoid Types

The tuberculoid types show three different histopathologic variations the typical miliary type with giant cells the sarcoidal type with circumscribed collections of hystiocytes of the foamy type in the form of round oval or sausage shaped nests and a third type with peculiar features ending in necrosis which we have described as lazard leprosy In the peripheral nerves the histologic changes [illegible] and there is a particular type reported by Eduardo Rabello Jr as nodular colliquative neuritis in which necrosis and abscess formation are the main features together with typical tuberculoid follicular structure. This last mentioned type may possibly be the neural equivalent of the lazarine leprosy of the skin.

Eduardo Rabello Jr has described tuberculoid changes of the sarcoidal variety in the lymphatic glands and bones a syndrome difficult to differentiate from lymphogranulomatosis benigna or Besnier Boeck Schaumann disease.

Clinically the tuberculoid lesions of the skin and peripheral nerves may be diagnosed by the expert As a rule the lesions are few in number sharply circumscribed erythematous patches or flat infiltrations often ring-shaped or festooned with macular centre and elevated border the latter being uniform or composed of small nodules arranged side by side.

Sometimes the lesions which are first infiltrated and elevated patches of vivid red or purple, suffer a process of involution in the centre and become atrophic with a ring like border The nerves more often affected are those of the upper extremities particularly the ulnar and also the superficial auricular branch of the cervical plexus. They appear as thick pencil like lineal infiltrations under the skin but show no discoloration. The ulnar nerve may be palpated in the ulnar canal at the inner part of the elbow as a thick or moniliform cord. In

the type described by Eduardo Rabello Jr , of which we have seen only one case, the painless abscess forms in the mass of the ulnar nerve and progresses toward the skin adhering to the latter and finally causing superficial necrosis and ulceration

Bacteriologically the lesions of tuberculoid leprosy show very few acid-fast bacilli Often only one or two bacilli may be seen in a whole section of skin or nerve after painstaking search often no bacilli at all can be demonstrated, either in the sections or in the lymph, tissue scrapings or mucous membrane secretions

Immunologically the tuberculoid types of leprosy show the maximum possible allergy of the skin in the form of strongly positive lepromin tests, varying from the nodular to the necrotic This is a constant feature which shows the excellent defenses of the body and proves once more the law of Jadassohn-Lewandowsky

From a prophylactic point of view, persons with tuberculoid leprosy are not dangerous and in some countries where leprosy is endemic these patients are not isolated but are allowed to remain at home under sanitary supervision. Some leprologists contend that these patients should not be treated but allowed to develop their reactions spontaneously

In 'lazarine leprosy' the clinical lesions consist of plaques of cutaneous gangrene developing at the site of bullae, these necrotic manifestations are few in number but extremely destructive, causing deep, foul ulcers usually in the extremities, which disorganise the muscles, tendons and joints These ulcers are painless and as a rule heal, leaving irregular scars in which there is absence of thermic and painful sensations Recurrent crops of bullae may occur after healing These are the only clinical manifestations, there being no other cutaneous or neural lesions of tuberculoid type The peculiar feature of this type of tuberculoid leprosy is that in spite of the tuberculoid structures of the affected tissue the gangrenous parts and the contents of the bullae are extremely rich in Hansen bacilli but not the tissue The lepromin test is strongly positive, showing a high allergic reaction indicative of excellent defenses In our opinion the 'lazarine' type of leprosy is the result of a massive infection with Hansen bacilli of patients with high immunologic defenses and the clinical symptoms represent the typical Koch phenomenon, with the throwing off of huge numbers of Hansen bacilli by the defensive mechanism of the body Lazarine leprosy, although highly destructive, is of good prognosis and most patients recover spontaneously

The Non-specific Types

Clinically the non-specific types of leprosy are characterised by the presence of macular, erythematous, achromic or pigmented skin lesions and by slight enlargement of the peripheral nerves with area of apparently healthy skin in which the thermic and painful sensations are abolished These types are at times exclusively neural and then the sole manifestations may be those due to trophic disturbances, such as areas of anaesthesia, muscular atrophies, retraction of the fingers and toes, paralysis of the muscles of the face, bone reabsorptions, mal perforans plantaris, disturbances of sweat and sebaceous secretions and falling of the hair More often neural disturbances and cutaneous erythematous or dyschromic lesions are present together Pathologically the tissues show only perivascular and perineural simple inflam-

natory changes consisting of cuffs of lymphocytes around the larger ressels of the upper cutis or the small trunks of the cutaneous nerves. In the cutaneous dyschromic or erythematous manifestations often called leprids there is also pronounced vascular dilatation and passive congestion The basal cells are often devoid of pigment and chromatophores may be very abundant on the upper cutis in the pigmented lesions.

Bacteriologically these lesions whether of the skin or of the nerves are poor in acid bacilli As a rule direct examinations of lymph result in negative findings

The lepromin test is negative in some cases and positive in others about 50% of each, although some investigators claim the numbers of positives much higher

In reality cases of non-specific leprosy are transitional types some of which progress toward the lepromatous type and others toward the tuberculoid types. At times the transition is quite rapid and a patient who shows only macular lesions will suddenly develop crops of lepromas in an acute outbreak of lepra reaction

The prognosis of these transitional types may be foretold by the results of the lepromin test. Those who show positive tests will probably remain as non-specific types or will develop tuberculoid lesions. Those showing a negative lepromin reaction will in all probability develop lepromatous lesions.

The Mixed Types

These transitions naturally result in types in which both lepromatous or tuberculoid and non-specific leprids co-exist until the patient finally develops the definite type which the disease will follow in his particular case. Therefore in these cases the presence of lepromatous establishes the type as lepromatous in spite of the presence of numerous erythematous or dyschromic lesions. Likewise the presence of tuberculoid lesions establishes the type as tuberculoid in spite of the presence of erythematous or dyschromic manifestations In many cases the clinical appraisal may be difficult and resort must be had to pathologic and bacteriologic examinations and even to the lepromin test in order to classify a case in the proper type.

The presence of lepromatous and tuberculoid lesions in the same patient has not been observed by us. The transformation of a lepromatous type into tuberculoid type or *vice versa* has been reported by several investigators but we have not seen this phenomenon.

Lepra Reaction

In sharp contrast with the usual slow and insidious evolution of leprosy there is sometimes observed an acute inflammatory phase which very frequently interrupts its chronic course or is the first clinical manifestation of the disease.

The major characteristic of the lepra reaction is its acuteness more or less accentuated in different cases. It is probably a manifestation of allergy or hyper-sensitivity of the body to the pathogenic agent. Sometimes the outbreak of the lepra reaction can be ascribed to a definite cause complicating diseases alimentary or alcoholic excesses too intensive antileprotic treatment and so on Frequently

it is impossible to determine its cause. The clinical picture and evolution of lepra reaction differ in lepromatous and tuberculoid cases

In lepromatous leprosy it generally begins suddenly with fever (39 to 40°C or 102 2 to 104°F) rigors, arthralgias, headache or prostration, followed in several hours by an eruption of erythema multiforme or erythema nodosum type and the exacerbation of pre-existing lesions In some cases there are extracutaneous symptoms adenitis, orchitis, splenic and hepatic enlargement, neuritis and keratitis The fever is of remitting type, and the other symptoms persist during several days, ten to fifteen, rarely more, and then disappear in lysis Relapses are frequent. The lepromin test is negative The erythrosedimentation index is greatly augmented Short, acute reactions are of good prognostic significance

Long or relapsing reactions aggravate the course of leprosy

The first therapeutic measure is the cessation of all antileprotic treatment and the administration of a mild saline laxative and a bland diet.

Injections of antimony and potassium tartrate 1% solution, calcium salts, vitamin B_1 and diphtheria toxoid are useful agents

Exacerbations in tuberculoid leprosy are not accompanied by any general symptoms or fever They are characterised by the turgescence of pre-existing lesions, the appearance of new wine red, infiltrated patches mostly located on the face and extremities, by a protracted course, never less than three months, and frequently more than a year in length The lepromin test is positive The erythrosedimentation index is always low and prognosis is always good

The Histamine Test

The early manifestations of leprosy of the non-specific or simple inflammatory type may be difficult to diagnose, although, if thermal and pain anaesthesia are present, matters are simplified However, many patients, especially children, do not co-operate or they find it difficult to express their sensations, in which event the performance of the 'histamine test' is very valuable.

When a drop of a 1 1,000 solution of a histamine salt is placed on the normal skin and a needle-prick is made through the liquid, a small wheal surrounded by an erythematous halo develops within a few seconds and persists for five minutes or more When the sensitive nerve endings are paralysed or destroyed, the phenomenon occurs as far as whealing, but no erythematous halo develops around the wheal The normal response to histamine is called the 'positive test', the absence of erythematous reaction around the wheal characterises the 'negative test' Therefore in the cutaneous lesions of leprosy the histamine test is always negative We have found occasion to do this test in numerous cases in which erythematous or dyschromic lesions were suspected of being early manifestations of leprosy The superficial, erythematonodular, cutaneous syphilids have been the subject of differential diagnosis with early lesions of leprosy in several cases, and in these the 'histamine test' has proved of definite help The serologic reactions may be positive in the presence of leprosy, and the changes in cutaneous sensations may be difficult to appraise when patients are not co-operative.

The Lepromin Test (Mitsuda Reaction)

The lepromin test consists essentially in the intradermal injection an antigen prepared from lepromatous tissues rich in Hansen illi.

Skin tests in leprosy were originally intended to find a diagnostic ocedure similar to the tuberculin test in tuberculosis. No results re obtained in this direction, and investigations were given up until 23 when Mitsuda reported that when an emulsion prepared with promatous skin was inoculated healthy persons gave positive results aculoanesthetic patients presented a late nodular persistent inflam ation and tuberous patients gave a negative local reaction He duced from his experiences that persons without leprosy and aculoanesthetic patients had a special immunity to the infection hile tuberous patients had no immunity These findings and con usions were later fully confirmed by many investigators.

All attempts to consider the test of any value in diagnosis are efinitely abandoned. Its great importance in the classification of ases of leprosy and its immunitary and prognostic value are actually ecognised by all.

Lepromin is prepared by boiling lepromatous tissues in isotonic olution of sodium chloride for one hour The mass is then ground p in a mortar and 20 c.c. of isotonic solution of sodium chloride is dded for each gram of ground up tissue. After thorough mixing and rinding again the supernatant fluid is pipetted off filtered through auze and stored in a sterile container the remaining tissue being liscarded.

The liquid is autoclaved at 120° C. for fifteen minutes phenolised at 0·5% and distributed in insulin type vials ready for use. It is a cloudy milky emulsion containing numerous bacilli and globi plus all the tissue elements of the leproma Kept in a dark cool place it retains its activity for a long time. No easy standardisation of lepromin is possible being as it is such a complex suspension of bacilli and tissue material, but this does not interfere with the accuracy of results as wide variations in the concentration of the antigen do not give correspondingly different reactions. A non reacting patient to the usual lepromin will not react to an antigen two or three times stronger A reacting patient will do so to dilutions as high as 1 3 000 of lepromin although with less intensity The presence of bacilli is essential to the activity of lepromin. Filtered antigens are inactive. Lepromins prepared with tuberculoid tissues (paucibacillary) produce attenuated reactions and then only in patient with strong reactions to the usual lepromin. Antigens prepared with normal skin are inactive.

The test is performed by injecting into the cutis 0·1 c.c. of lepromin The most common sites used are the arms the dorsum and the anterior surface of the thigh. At the end of twenty four to forty-eight hours an erythematous halo may be observed with, at times some infiltration but these manifestations disappear quickly usually after the fifth day leaving a dark brown discoloration and some wrinkling of the skin. On the seventh to the tenth day a small papule begins to form in the positive cases gradually increasing in size and reaching its acme about the third to the fourth week when it may be a nodule of as much as 1 cm. in diameter Occasionally the centre sloughs off and a small ulcer forms which requires several weeks to heal. In most cases the nodule regresses gradually after the fourth week, but

in some cases of positive reaction some scarring is left. Rarely a positive reaction may not show until the third or fourth week and then follow the usual regressive course

The erythematous reaction of the first few days is considered non-specific The reading of the test should be done about the thirtieth day after the intradermal injection If there is no reaction or only a small (less than 5 mm) infiltration the test is negative A well-formed nodule more than 5 mm in diameter with or without a necrotic centre characterises the positive test

Microscopic examination when the Mitsuda reaction is positive shows in specimens removed at its acme a collection of histiocytes, lymphocytes and at times giant cells, with an aspect very similar to that of tuberculoid leprosy In specimens removed forty-eight hours after inoculation acute inflammatory phenomena may be observed without any specific changes, but in some of our specimens a decided perivascular histiocytic infiltration was present, resembling even at this early date the tissue changes of tuberculoid leprosy However, we do not believe this is of diagnostic significance, as we have observed similar changes in lepromin tests of forty-eight hours' duration which later proved to be negative The injected bacilli are not demonstrable in the lepromin reacting tissues In negative tests, after the initial inflammatory reaction biopsies performed after eight, fifteen and twenty-eight days showed a return of the tissues to normal

COMMENT

1 The classification of the types of leprosy on a histopathologic foundation into 'lepromatous' 'tuberculoid' and 'non-specific' is the result of studies made by dermatologists of Brazil and Argentina, and accepted by Latin American dermatology In this article an attempt is made to correlate these pathologic forms with the clinical, immunologic bacteriologic and public health aspects of the disease

The lepromin test is given an important place among the immunologic reactions of the skin and reports are made based on many tests performed by the authors, corroborating for the most part the findings of other investigators

The histamine test is studied as a diagnostic procedure in early cases of leprosy with lesions of the 'non-specific' type

TREATMENT OF PERFORATING ULCER OF THE FOOT

By E Muir LL D M D M R C S E

[*Reprinted from Leprosy Review* 1943 14 49]

Much has been written on this subject, and the writer s apology for adding to the literature is that he has recently had considerable experience of this condition which is among the three most common and important complications of leprosy

Definition

Perforating ulcer differs from the other form of ulcer found in leprosy commonly called lepromatous (*a*) in not being due to the local presence of M. leprae, (*b*) in being a sequela of impaired trophic and sensory supply to the foot or the part of the foot involved (*c*) in being confined to the sole of the foot while lepromatous ulcers are found on other parts of the body surface.

Causation

The destruction or blocking of the sensory nerves primarily by cellular pressure on and later by fibrous constriction of the axis cylinders deprives the foot of sensation and trophic supply and to a certain extent involves the vascular supply The motor nerve supply is also affected when the disease spreads to the larger mixed nerves

It is difficult to dissociate these four elements. We are all familiar with the temporary feeling of paralysis of the lower lip when an anaesthetic has been injected for extraction of a tooth from the lower jaw By comparison it is easy to understand the paresis of the small muscles of the face, hand and foot when leprosy causes anaesthesia of the covering skin an anaesthesia which,lasts not for a few hours as in the dental extraction but for months and years. Thus the small muscles of the foot deprived of their normal sensory stimulus become paretic, and fibrous tissue takes the place of muscle fibre.

These muscles normally support the arches of the foot and act as padding between the bones and the ground. They give elasticity to the foot and their tension keeps the bones of the foot strong and hard. All these functions are impaired by anaesthesia of the foot, and the muscles are further affected by interference with the motor supply and all the parts skin joints and muscles are further weakened by interference with the trophic and vascular supply

In this weakened condition of the foot a small injury is sufficient to initiate what is known as a trophic or perforating ulcer Such injuries are the more liable to occur as the protective influence of sensation is withdrawn and the patient may be unaware of an abrasion caused by rubbing of the shoe or the perforation of a sharp stone thorn or nail.

The ulcer may at first be superficial but if not attended to at once it tends to affect the deeper structures and penetrate to the bone. Septic infection complicates the process the soft and decalcified bone becomes carious and an abscess of the foot may occur which, after a few days may be discharged through the perforation.

Treatment

Perforating ulcers may be divided into two groups superficial and deep, the bone being affected in the latter

Superficial ulcers generally show the qualities common to all chronic ulcers a septic floor surrounded with raised, sclerosed non-vascular edges Demobilisation with the application of the usual poultices and antiseptic dressings may cause healing, and this process may be accelerated by infiltration into the surrounding subcutaneous tissue of a mildly irritant fluid, such as hydnocarpus oil (1 to 2 c.c) or a 1 in 4 solution of Dettol (1 to 2 c.c), which causes exfoliation of the thick surrounding cuticle

When the bone is involved its removal is essential, and it will be found wise to reverse the usual surgical rule and not be too conservative in the amount removed

While perforating ulcers may occur anywhere in the sole of the foot, by far the commonest sites are the heads of the metatarsals, the first metatarsal being that most commonly involved

While a more conservative operation may suffice in the slighter cases, the operation of choice is complete metatarsectomy This causes narrowing of the foot, but the result is much more likely to be permanent There is nothing more damaging to the health and confidence of the patient than an ulcer which recurs whenever he begins to walk again

Metatarsectomy

The writer recommends the following technique which he has found simple, rapid and satisfactory in its results An anaesthetic is seldom necessary as sensation is almost entirely absent The patient lies on the table with his foot projecting and the end of the table supporting his *tendo archilles* After the parts have been thoroughly cleaned and iodine has been applied, a tourniquet is applied firmly over a piece of lint round the middle of the thigh Sterile towels are arranged so that only the distal part of the foot is uncovered An incision is made in the sole beginning at the ulcer, extending for the whole length of the metatarsus and cutting down to the bone The bone is quickly cleared, as is also the proximal phalanx if it is involved A small cutting bone forceps is useful in disarticulating the bone and disengaging it from its bed When the bone has been removed the sides of the ulcer are dissected out and the wound is trimmed, the edges being undercut and freed so that they come together, if possible, without tension Sulphanilamide powder is rubbed thoroughly into the wound Sterile gauze is inserted sufficient to stop bleeding but not to prevent the approximation of the edges, the end of the gauze projects through the dependent end of the wound The wound is closed with a few strong, deep sutures, and over an outside dressing a tight bandage is applied The tight packing of gauze, the sutures and the tight bandage do away with the necessity of applying ligatures, thus saving much time The whole operation may be finished in 15 to 20 minutes, and this is important as the patient generally begins after that time to complain of the pressure of the tourniquet This is removed as soon as the first few turns of the bandage have been made The sulphanilamide powder keeps the wound clean, so that the first change of dressing can be delayed for forty-eight hours, by which time

the danger of bleeding is past The gauze is removed and a thin wick of gauze powdered with sulphanilamide powder inserted

The wound generally takes about three to four weeks to heal but the patient should not apply his foot to the ground for a further four weeks so as to give the fibrous tissue time to consolidate

After the first forty-eight hours the patient should be encouraged to walk about on crutches, keeping his foot carefully off the ground

The last two rules are indeed important in the treatment of all perforating ulcers even when an operation has not been necessary

When a perforating ulcer occurs as is less often the case in connection with the heel operative measures are less satisfactory If rest dressings and infiltration of the subcutaneous tissue round the ulcer *do not bring about a permanent cure* a layer of the bone in the base of the wound may be gouged out and the edges undermined, trimmed and brought together as described in the operation above.

After operation or in simple cases where operation is not necessary unless the healed wound has time to consolidate (generally 3 to 4 weeks), it is likely to recur but the use of crutches removes the need for confinement to bed which is so harmful to the general health and interferes with the beneficial effects of exercise in the treatment of leprosy

In many cases the writer has found the progress of the patient handicapped *or altogether stopped* by the *demobilisation* attendant on perforating ulcers as well as by septic absorption from the wound On this account he considers it imperative that immediate steps should be taken to effect permanent healing Much can be done to prevent the occurrence of perforating ulcer by the use of proper footwear the application of suitable padding inside the shoes and careful hygiene of the feet. When anaesthesia of the feet occurs the patient should be warned before hand of the dangers and taught how to avoid them.

REPORTS

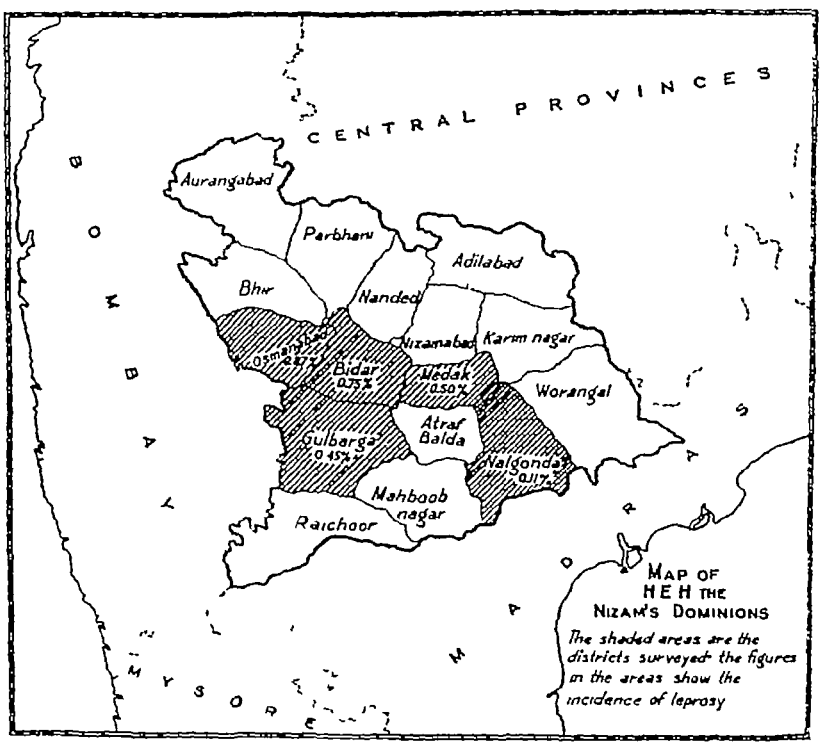
REPORT ON LEPROSY SURVEYS IN HYDERABAD, DECCAN

By A SHAMA RAO, *Leprosy Officer, H E H The Nizam's Government*

INTRODUCTION

In the year 1929 under the auspices of B E L R A Indian Council, a leprosy survey was conducted by Rai Sahib Dr I Santra in Nizamabad Taluk, and 538 cases of leprosy were found in a population of about 60,000 giving an incidence of 88% Dr Santra again visited Hyderabad in 1940 and surveyed 57 villages in the four districts of Bidar, Gulbarga, Osmanabad and Raichur 635 cases of leprosy were detected in a population of about 60,000 giving an incidence of 1% The incidence in the different districts varied from 8% to 1 6%

In 1943 the Nizam's Government sanctioned a scheme of leprosy survey of Hyderabad for two years A Leprosy Survey Officer has been appointed, and villages in five districts have so far been surveyed The findings made during the surveys are reported below



General remarks on the methods of survey

Surveys were carried out in the villages lying within a radius of five miles from an existing leprosy clinic attached to a hospital or

dispensary House to house visits and clinical examination of cases and their contacts were made. The advantages of treatment of early cases, and the importance of isolation of infectious cases were impressed upon the public. Printed hand bills in vernacular explaining the nature of leprosy its early signs and symptoms and the methods of prevention and isolation, were distributed. Magic lantern lectures were given in bigger villages Clinic Committees were formed where the incidence was found to be high and the influential people were willing to co-operate and to undertake the responsibility of sending the registered cases for treatment regularly to the Government clinic every week and adopt suitable measures for isolation of infectious cases.

THE FINDINGS MADE.

The findings made in the different districts will be given district by district and then the main findings made in all the districts will be given together

OSMANABAD

No of villages surveyed and area.	Total population	Cases detected.			Percentage of L cases	Incidence.
		N	L	Total		
Villages 70 Area 340 sq miles.	53,450	317	145	462	31 39	0 87%

Type age and sex distribution

Age group	Cases.						Total for age groups.			Per centage of L cases.	Percentage in age group
	N			L							
	M	F	T	M	F	T	M	F	T		
0–14	44	14	58	6	2	8	50	16	66	12 12	14 28
15–34	110	34	144	45	18	63	155	52	207	30 43	44 81
35 and over	90	25	115	52	22	74	142	47	189	39·15	40·91
TOTAL	244	73	317	103	42	145	347	115	462	31 39	100·00

BIDAR.

No. of villages surveyed and area.	Total population	Cases detected			Percentage of L cases	Incidence.
		N	L	Total		
Villages 27 Area 136 sq miles.	19 426	122	24	146	16·44	0·75%

Type age and sex distribution

Age group	Cases						Total for age groups			Per-centage of L cases	Percentage in age group
	N			L							
	M	F	T	M	F	T	M	F	T		
0–14	18	3	21				18	3	21	Nil	14 38
15–34	24	20	44	7	2	9	31	22	53	16 98	36 30
Over 34	40	17	57	13	2	15	53	19	72	20 83	49 32
TOTAL	82	40	122	20	4	24	102	44	146	16 44	100 00

MEDAK

No of villages surveyed and area	Total population	Cases detected			Percentage of L cases	Incidence
		N	L	Total		
Villages 35 Area 172 sq miles	34 386	127	45	172	26 16	0 50%

Type age and sex distribution

Age group	Cases						Total for age groups			Per-centage of L cases	Percentage in age group
	N			L							
	M	F	T	M	F	T	M	F	T		
0–14	11	6	17	3	1	4	14	7	21	19 05	12 21
15–34	21	14	35	5	3	8	26	17	43	18 60	25 00
Over 34	54	21	75	28	5	33	82	26	108	30 56	62 79
TOTAL	86	41	127	36	9	45	122	50	172	26 16	100 00

NALGONDA

No of villages surveyed and area	Total population	Cases detected			Percentage of L cases	Incidence
		N	L	Total		
Villages 41 Area 224 sq miles	41 594	30	18	48	37 50	0 11%

Type age and sex distribution

Age groups	Cases						Total for age groups			Per centage of L cases	Percentage in age group
	N			L							
	M	F	T	M	F	T	M	F	T		
0–14	3	2	5				3	2	5	Nil	10 42
15–34	1	1	2	4		4	5	1	6	66 67	12 50
Over 34	21	2	23	11	3	14	32	5	37	37 84	77 08
TOTAL	25	5	30	15	3	18	40	8	48	37 50	100 00

GULBARGA

No of villages surveyed and area.	Total population	Cases detected.			Percentage of L cases.	Incidence
		N	L	Total.		
Villages 59 Area 250 sq miles.	51 770	171	63	234	26·92	0·45%

Type age and sex distribution

Age groups.	Cases.						Total for age groups			Per centage of L cases.	Percentage in age group
	N			L							
	M	F	T	M	F	T	M	F	T		
0–14	21	5	26	2	2	4	23	7	30	10 33	12 82
15–34	44	14	58	18	7	25	62	21	83	30 12	35 47
Over 34	58	29	87	29	5	34	87	34	121	28·09	51·71
TOTAL	123	48	171	49	14	63	172	62	234	26·92	100·00

The main findings for all the five districts are given in the following table —

District surveyed.	Number of villages surveyed.	Total population	Total number of cases.	Incidence	Per centage of L cases	Per centage in children of 15 and under
Osmanabad	70	53 450	462	0 87%	31 39	14·28
Bidar	27	19,426	146	0·75%	16 44	14 38
Medak	35	34 386	172	0·5%	25 16	12 21
Nalgonda	41	41 594	48	0·11%	37 5	10·42
Gulbarga	59	51 770	171	0·45%	26·92	12 82

SOME COMMENTS ON THE ABOVE FINDINGS

The incidence.

The incidence of the disease varies from 11% in the district of Nalgonda to 87% in the district of Osmanabad

Type distribution

The proportion of lepromatous cases varies from 16% in the district of Bidar to 37% in the district of Nalgonda. It will be noted that in the district of Nalgonda the incidence of the disease is lowest while the proportion of the lepromatous cases is highest however the number of cases in Nalgonda is very small 48 Of the remaining 4 districts Osmanabad has the highest incidence that is 87% and also the highest proportion of lepromatous cases that is 31 3%

Age distribution

The proportion of cases in children below the age of 15 varies from 10% in the district of Nalgonda to 14·3% in the district of Osmanabad Thus in all the districts surveyed the proportion of cases in children is rather low

Sex distribution

About 75% of the cases detected have been in males, that is, the proportion of cases in males and females is about 3 to 1 *

Conclusions

In view of the above findings, it is considered that leprosy is not a serious problem in the areas surveyed †

SOME GENERAL INFORMATION ABOUT THE AREAS SURVEYED

The following table gives some general information about the areas surveyed —

District	Racial	Altitude	Rain-fall	Climate	Main crop
Osmanabad	Marhatawada District	2000′	36″	Cool and dry	Jowar wheat and ground-nuts
Bidar		2000′	36″	Cool and dry	Jowar ground nuts and rice
Gulbarga		1300′ to 1800′	26″	Hot and dry in summer, cool in winter	Jowar bazra and ground-nuts
Medak	Telengana District	1700′		Humid in winter due to presence of irrigation tanks dry in summer	Jowar maize, rice and pulse
Nalgonda	,	800′ to 1200′	25″	Do	Jowar bazra and rice

* These figures cannot be accepted as truly representing the sex distribution of the disease because of the prevalence of the purdah system and the absence of facilities to examine ladies —EDITOR *Leprosy in India*

† Although the incidence and the proportion of cases in children is not very high yet the proportion of lepromatous cases in most of the areas is fairly high We do not consider that the statement that leprosy is not a serious problem in this area is quite justifiable —EDITOR *Leprosy in India*

EPIDEMIOLOGICAL LEPROSY SURVEYS IN BIHAR

By DR I SANTRA

Selection of the areas

The districts of Manbhum and Santal Parganas were selected for carrying out intensive epidemiological surveys in selected areas. The district of Manbhum was selected because the District Board Manbhum has been engaged for the last three years in carrying out intensive leprosy surveys and it was proposed to survey an area in the district that had already been surveyed by the District Board workers, and to compare the previous findings with the findings made in this survey Chirkunda was selected for this purpose The time taken by the District Board authorities to select Chirkunda was utilised in surveying the village Raghabpur in District Manbhum a village near Purulia.

The District of Santal Parganas was selected with the special object of carrying out surveys amongst Santals. A survey carried out in 1940 in a Santal colony in Jalpaiguri district in Bengal had given some unusual findings and it was proposed to survey an area in Santal Parganas reserved for Santals and Paharias to find out what was leprosy like in the home districts of the Santals.

The findings made

A relatively small number of persons has been examined in village Raghabpur A summary of the findings made in this village will be given first the findings made in the other two areas will then be considered in detail. At the end a comparison will be made of the findings made in the three areas.

Raghabpur Manbhum District

Gross findings

Population examined.	Cases found			Incidence %	Proportion L cases %
	N	L	Total.		
1 595	51	12	63	3·94	19

Age type and sex distribution of the cases

Age	Neural.			Lepromatous			Total for age groups.				Per cent. of cases in the age groups.
	Male.	Female	Total.	Male.	Female.	Total	Male	Female.	Total.	% L.	
0–14	4	1	5	0	0	0	4	1	5	0	7·93
15–34	15	7	22	5	2	7	20	9	29	24	46·03
35 and over	11	13	24	5	0	5	16	13	29	17	46·03
TOTAL	30	21	51	10	2	12	40	23	63	19	99·99

Chirkunda, Manbhum District

Gross findings

Population	Number examined	Cases detected			Incidence %	Proportion of L cases %
		N	L	Total		
Total	5 192	134	23	157	3 02	14 64
Adult	3 201	106	23	129	4 03	17 05
Children	1 991	28	0	28	1 40	0 0
Male	2 618	68	14	82	3 13	17 07
Female	2 574	66	9	75	2 91	12 0

Age and type distribution of cases

Age group	N	L	Total.	Proportion of L cases	Percentage of total cases in the age groups
0–14	28	0	28	Nil.	17 83
15–34	46	12	58	20%	36 94
Over 34	60	11	71	15%	45 22
TOTAL	134	23	157	14 64%	99 99

Sex age and type distribution of cases

Age	Neural			Lepromatous			Total for age groups				Proportion of male cases in the age group
	Male	Female	Total	Male	Female	Total	Male	Female.	Total	% L	
0–14	13	15	28	0	0	0	13	15	28	0	46 43%
15–34	23	23	46	5	7	12	28	30	58	20	28 27%
35 and over	32	28	60	9	2	11	41	30	71	15	57 74%
TOTAL	68	66	134	14	9	23	82	75	157	14 64	52 22%

Incidence by caste

Caste	Population examined	Incidence %	L rate %
Santals	800	2 5	25
Depressed class (Bauri Bagdi Hadi, Chamar Mullick)	2 060	3 05	19 04
Middle Class Hindus (Chasa, Gowala Ghatwal Sundi Napit)	1 419	4 15	8 47
Brahmins and Kayasthas	247	2 02	0
Mohammedans	662	1 51	10

The outstanding points are as follows —

The incidence of 3 13% is fairly high but the proportion of epromatous cases 14·6% is rather low The proportion of cases in children is 17 83% The two sexes are about equally affected

A comparison of the present findings with the findings made by the District Board in 1940 in the same area.

	Population examined	Cases			Incipient or doubtful cases
		N	L	Total.	
1940	5 204	93	36	129	25
1943	5 192	134	23	157	11

Of the present 157 cases only 91 were included in the previous survey Ten cases have since come to the area and as many as 56 cases represent the new cases since arisen and the cases missed in the 1940 survey On general grounds one would not expect such a large number of new cases arising in a population of this size during the course of three years It would therefore appear that the findings of the 1940 survey were not very accurate.

Progress and fate of the cases detected in 1940

Out of the 25 *incipients*

5 are new cases of the neural type.
1 still doubtful.
14 show no signs.
5 could not be traced said to have left the area

Out of the 93 *neurals*

2 have turned lepromatous
9 show no signs.
6 have died.
10 have left the area
66 are recorded *in* 1943 as neurals.

93

Out of the 36 *lepromatous cases*

2 are found to be Nt.
1 is now bacteriologically negative
6 have died.
6 have left the area.
21 are recorded as L cases in the 1943 survey

36

Hiranpur, Santal Parganas

Gross findings

Population	Number examined.	Cases detected.			Incidence %	Proportion of L cases %
		N	L	Total		
Total	4 991	92	11	103	2 06	10 67
Adults	3 104	81	11	92	2 96	11 95
Children	1,887	11		11	0 58	0 0
Male	2 533	48	7	55	2 17	12 72
Female	2 458	44	4	48	1 95	8 33

Age and type distribution of cases

Age groups	N	L	Total	Proportion of L cases %	Percentage of total cases in the age groups.
0–14	11		11		10 68
15–34	31	8	39	20	37 83
Over 34	50	3	53	5 65	51 45
TOTAL	92	11	103	10 67	99 96

Sex age and type distribution of cases

Age group	Neural.			Lepromatous			Total for age groups				Proportion of male cases in the age groups %
	Male	Female	Total	Male	Female	Total	Male	Female	Total	%L	
0–14	3	8	11	0	0	0	3	8	11	0	27 27
15–34	17	14	31	5	3	8	22	17	39	20	56 41
35 and above	28	22	50	2	1	3	30	23	53	5 65	56 6
TOTAL	48	44	92	7	4	11	55	48	103	10 67	52 72

Leprosy in the different races

The population of Hiranpur is composed of the following racial groups —

	Population
Santals	3,472
Paharias	1,295
Others	224
TOTAL	4,991

It will be seen that there are two main groups, the Santals and Paharias. There are racial, linguistic and social differences between these two groups The Paharians live on top of hills, because of scarcity of water they do not keep their homes clean nor do they

bathe regularly and they eat dead bodies of animals. The Santals who live in villages are more clean and do not eat the dead bodies of animals. It would be interesting to compare the findings made in these two groups

	Population examined.	Cases of leprosy			Gross incidence %	Proportion of L cases %	Proportion of cases in children %	Proportion of cases in males %
		N	L	Total.				
Santals	3,472	68	8	76	2 18	10·5	8	49
Paharias	1,295	21	3	24	1 08	12 5	17	58

In Santals the incidence of leprosy is double of that in Paharias However the proportion of lepromatous cases, and the proportion of cases in children are lower especially the proportion of cases in children which is half of that of Paharias

Leprosy in Santals

In a survey made in 1940 in a Santal colony in Bengal (Santalpur Jalpaiguri district) some unusual findings were reported with the gross incidence of leprosy of over 7% the proportion of lepromatous cases was only 4% The question arose whether this type of finding was characteristic of the Santals as a race. The findings made during the present surveys amongst the Santals do not lend support to this view The findings made among the Santals in the three areas are compared in the following table —

	Proportion examined.	Incidence.	L rate	Male rate	Child rate
Santalpur (Jalpaiguri district, Bengal)	3 600	7 40	4 1	53	17
Hiranpur (Santal Parganas Bihar)	3 472	2 18	10·5	49	8
Chirkunda (Manbhum district Bihar)	800	2 5	25·0	52	18

It will be noted that the findings made at Santalpur are not at all characteristic of the Santals as a race.

Comparative findings for the three areas

The findings made in the three areas are summarised in the following table —

	Persons examined.	Incidence %	L rate	Male rate	Child rate
Raghabpur	1 598	3·94	18	64	8
Chirkunda	5 192	3·02	14·64	52	18
Hiranpur	4 991	2·06	10·6	53	11
TOTAL	11 781	2·74	14·24	55	14

EPIDEMIOLOGICAL LEPROSY SURVEYS IN THE CENTRAL PROVINCES

By DR I SANTRA

Areas selected

Two areas were selected in the C P fairly widely separated and inhabited by different kinds of people, the social and economic conditions also showing considerable differences The areas selected were Kurud in the District of Raipur (Chattisgarh Division), and Kashikhed in Amraoti (Berar) It was expected that most of the cases in the two areas selected were already known, since there is a considerable amount of anti-leprosy activities in both the areas In Kurud a leprosy survey was made in 1928, and a leprosy clinic was opened Since then every village is supposed to have been visited annually The present survey was done in the villages situated within 4 miles of the leprosy clinic A leprosy clinic was opened in Kashikhed in the year 1939 in response to efforts by the Kashikhed village uplift committee.

Time spent on the surveys

The surveys were done in 1942 and three months were spent at each place The local assistant health officers helped in the work

People in the two areas

The people at Kurud are Hindi speaking and rice eaters, while at Kashikhed they are Maharatti speaking and juar eaters Most of the people in Kurud are of the depressed or aboriginal class, and in them the family is a very unstable institution, and they are very superstitious people In Kashikhed the family is a stable institution, and the people are not so superstitious The Kashikhed people are better off economically and have better diet

The findings made

The findings made in the two areas will first be given separately, and then a comparison will be made of the findings in these two areas

KURUD

The Main findings made in Kurud are summarised as follows —

Gross findings

Population	Persons examined.	Cases			Incidence %
		N	L	Total.	
5 498	5 498	51	13	64	1 16

Incidence by age

	Examined.	Cases.	Incidence %
0–14	1 902	9	47
15–34	1 728	15	87
Over 34	1 868	40	2 14
TOTAL	5,498	64	1 16

Age-type-distribution of cases.

Age group.	Cases.			Proportion of L cases %	Percentage of cases in the age-group
	N	L	Total.		
0–14	8	1	9	11	14·0
15–34	9	6	15	40	23 5
Over 34	34	6	40	15	62 5
TOTAL	51	13	64	20	100·0

Age sex and type

	Examined.	Cases.			Proportion of L cases %
		N	L	Total.	
Males					
0–14	980	4	1	5	20
15–34	864	5	4	9	37
Over 34	830	18	6	24	25
TOTAL	2 674	27	11	38	29
Females					
0–14	922	4		4	0
15–34	864	4	2	6	33
Over 34	1 038	16	0	16	0
TOTAL	2 824	24	2	26	8

The outstanding points are as follows —

The incidence of 1 16% is not very high. Proportion of lepromatous cases 20% is fairly high. The incidence in females is 92% compared with 1 42% in males. The proportion of lepromatous cases in females is relatively much lower 8% compared with 29% in males, but the numbers are small. One striking feature is the

than is actually proved to be In the second area, Kashikhed, leprosy was known to be common and it is generally reported to have been increasing but an incidence as high as 4 84% was not expected Therefore in both cases the incidence figures are rather different from what was expected There are differences in the type-distribution of cases seen in the two areas, Kurud showing 20% of lepromatous cases while Kajikhed showed 8% It has been strongly suggested that the proportion of lepromatous cases is an important indication of the public health importance of leprosy and a high proportion may indicate that the disease is on the increase, but certain recent survey findings are not in keeping with this idea There is on the whole more evidence that the disease is on the increase in Kashikhed but the proportion of lepromatous cases here is definitely low

Another noticeable difference between the two areas is in the age-distribution of the cases In Kurud a low proportion of cases is in children and a high proportion of cases, no less than 62%, is above the age of 34, whereas in Kashikhed the proportion of cases in children is considerably higher and the proportion of cases in the older people is only about half of what it is in Kurud.

The age-distribution, it has been suggested, is an important indication of the severity of the leprosy problem, a high proportion of cases in children and a low proportion in old people being a serious finding suggesting that leprosy is increasing The results of the present two surveys would give some support to this idea

These two surveys do therefore raise some interesting epidemiological points, and suggest that a high proportion of cases in children and a low proportion in people of middle age and over is a more important indication that leprosy is on the increase than a high proportion of lepromatous cases Some other survey findings also point to this direction.

From the practical point of view these two surveys suggest that leprosy in the Kurud area may be an old long-standing, not very serious, and possibly diminishing problem, whereas in the Kashikhed area leprosy is more common and possibly or probably increasing It is not sure that the findings of these two surveys are entirely characteristic of these two areas but this seems not impossible, and if this is confirmed it may be an indication that there is more need for anti-leprosy work in Berar than in Chattisgarh

ANNUAL REPORT OF THE MADRAS PROVINCIAL BRANCH OF THE B.E.L.R.A. 1942 43

The Report opens with the remark that the work during the year has been affected to some extent by the prevailing war conditions but that since the Government realises the importance of anti leprosy work in the presidency the activities of the Association have been hampered as little as possible. The work of the Association is carried at the following investigation centres —

1 Head office, the Lady Willingdon Leprosy Sanatorium Chingleput.
2 Saidapet Childhood Leprosy Control Investigation centre.
3 Madras City Urban Leprosy Control Investigation centre.
4 Ettapur Childhood Rural Leprosy Control and segregation investigation centre.
5 Madurantakam Rural Leprosy Control Leprosy Investigation centre.
6 Madura, Cuddalore and Wandiwash centres

Dr R G Cochrane Chief Medical Officer Lady Willingdon Leprosy Sanatorium Chingleput, and Hon. Secretary of the Madras Provincial Branch directs the various lines of investigation but in charge of each investigation unit is a specially trained officer

The report describes the work done at the various centres.

1. *Saidapet Childhood Leprosy Control Investigation Centre Silver Jubilee Clinic Saidapet*

The work of this unit as in previous years has included (*a*) Epidemiological studies (*b*) Immunological work and (*c*) Clinical investigation.

(*a*) *Epidemiological studies* —

(i) During the year three fresh areas of Saidapet have been surveyed and a total population of about 5 000 has been surveyed. Table I gives the findings made in these areas together with the finding made in the two previously surveyed areas.

(ii) Figures were published three years ago indicating that contact appeared to be the most important single factor in the acquirement of leprosy The work since then has continued to emphasise this. From an up-to-date analyses of nearly three hundred children the following points which emerge are of interest. The open case contact in 69·7% of cases was traced to an intrafamilial or house contact. In 167 cases where the contact was maximal, that is room contact 32 3% developed the more benign form of the disease. The latter figure is of interest for it indicates that even under the conditions most favourable for the acquirement of leprosy one-third of the cases apparently develop only benign forms. A further analysis therefore of the family history of these 167 cases has been undertaken in 141 of these, satisfactorily accurate details were available It is of interest to note that 70 open cases infected these 141 children but that the total number of children exposed to the infection by close and intimate contact was 225 that is 62 7% developed the disease. The remaining 37 3% had no signs of the disease but it is admitted that some of these cases may still develop leprosy in later years.

TABLE I

Comparative study of survey findings

	Areas previously surveyed.						Fresh areas surveyed.								
	Area A			Mambalam village.			Srirampet & Eddapalayam.			Area B			Pempet.		
	Total.	Male	Female.	Total.	Male.	Female.	Total.	Male.	Female.	Total.	Male.	Female.	Total.	Male	Female.
Total population—adults	1 417	706	711	690	349	341	694	334	360	2,116	1,135	981	432	227	205
Number examined—adults	1 283	624	659	553	244	309	574	263	311	2 071	1 097	974	380	202	178
Total population—children	794	410	384	413	214	199	398	226	172	1 093	557	536	250	123	127
Number examined—children	757	383	371	405	207	198	358	194	144	1 087	553	534	210	100	110
Number of cases detected—adults	70	37	38	16	9	7	25	8	17	100	67	33	9	5	4
Number of cases detected—children	67	35	32	12	10	2	7	6	1	91	49	42	6	4	2
Percentage of population examined	92 3%			86 9%			85 3%			98 4%			86 6%		
Gross incidence	67·1 per 1000			29 8 per 1000			35 0 per 1000			60 4 per 1000			25 4 per 1000		
Child incidence	88 5			29 6			20 7 ,,			83 0			28 57 ,		
Sex incidence—male	71 3 ",			42 0			30 6			70 3			29 9		
Sex incidence—female	63 1			17 8			39 6			49 7 ,			20 8 ,		
Sex rate	52 5%			67·8%			43 75%			60 73%			60 0%		
Child rate	48 8%			42 8%			21 9%			47·64%			40 0%		
Open case rate	24 8%			14 3%			12 5%			16 7%			26 6%		

(*b*) *Immunological work* The work on the lepromin test has been continued. In view of the fact that Dr Dharmendra of the School of Tropical Medicine Calcutta, has succeeded in preparing a bacillary antigen completely free from tissue material it is proposed, as opportunity arises to review the whole work using this new and refined lepromin.

(*c*) *Clinical investigation* Because of the unique material present at the Silver Jubilee Clinic the various clinical manifestations of the disease and its development are being thoroughly studied The lesions of leprosy in children fall into the following main categories the simple macules of incipient leprosy the simple macules of neural leprosy macules of tuberculoid leprosy and macules of lepromatous leprosy

While the macules of incipient leprosy tend to merge into those of simple neural leprosy and while the number of true incipient lesions is comparatively low (5%) it is felt that this variety is sufficiently important from the prognostic point of view to warrant its retention as a special variety of macular lesions.

It can be stated that the earliest lesions of leprosy is a macule but it should be of great value if we could separate from large group of hypopigmented macules seen in the skin of those which are lesions of very early leprosy and those in which such diagnosis can be excluded. This work is extremely difficult but at the Silver Jubilee Clinic there is a unique opportunity to investigate such lesions.

2 *Madurantakam Rural Leprosy Investigation Centre Polambakkam*

The work at the centre consists of epidemiological surveys and the control work.

(*a*) *Epidemiological studies* The routine survey has continued throughout the year and all the villages originally chosen and their Adi-Dravida colonies have been completed. This area was chosen as a result of preliminary surveys done some years ago because it was considered that the villages in the area had a higher incidence of leprosy than elsewhere in the district. Out of 35 villages (17 caste villages and 18 Adi-Dravida colonies) not less than 15 have a gross incidence of more than 30 per millem the highest incidence recorded is 76·9 per mille. It is admitted that some villages are only hamlets with very small populations and therefore a high gross incidence here may not have the same significance as in those villages where the population is greater and as a result the actual number of open cases is higher In seven out of the eighteen villages a fresh survey has been undertaken and Table II gives a comparison of the figures in the old survey with that of the new

(*b*) *Prevention* One of the chief aims of the Rural Investigation Unit is its endeavour to discover a method of control which is practicable and applicable to rural areas Night segregation has been continued throughout the year but it is difficult as yet to come to a conclusion with regard to the efficacy of night segregation It is true that the fewest new cases have arisen in the hamlet in which the incidence is highest and where night segregation has been most effective. The population of this area—Perambakkam Adi Dravida colony—is only 272 and the two new cases both non infective, are contacts of open cases who are now under night segregation

TABLE II

Comparative study of survey findings

Name of village	Date of survey	Incidence per mille	Child rate %	Open case %	New cases	Population.	REMARKS
Polambakkam	April 1939	41 15	30 0	26 66		734	Of the new cases one was not in the village in the last survey and two men recorded as suspicious in the previous survey
	May 1942	51 89	25 88	23 25	17	835	
Perambakkam	June 1939	38 46	14 28	28 57		370	One case came into the village since last survey and one was recorded as suspicious in the last survey
	June 1942	47 70	11 76	35 29	4	440	
Perambakkam Cheri	Sept 1939	78 12	50 0	30·0		128	One was recorded as probably incipient in the last survey, and one case absent when the last survey was undertaken
	June 1942	66 10	50 0	37 5	3	132	
Maluvankaranai	Oct, 1939	33 12	18 18	45 45		356	Two cases were reported as suspicious in the last survey one case was probably missed in the last survey and one case was absent in the last survey
	Feb 1942	48 84	23 53	29 41	8	374	
Maluvankaranai Cheri	Oct., 1939	33 98	57 14	42 85		235	Two cases were missed in the last survey One case was not included in the figures in the last survey although a note on the case was made One case, a child has developed lesions possibly of incipient nature but the child is too young to be certain of a definite diagnosis
	Feb, 1942	56 33	38 46	30 77	8	261	
Mukundagiri	Oct 1939	11 46	50 0			356	No new infection have actually arisen in this village The case recorded was one which was not detected in the last survey
		14 57	40 0		1	357	

3 *Urban Investigation Centre Royapuram, Madras*

(*a*) A considerable amount of the work in the urban area was dislocated during the time of emergency in April last. Owing to the proximity of this area to the coast some 49% of the population have not returned and may have to be considered as evacuated for the duration of the war With this in mind the whole area was re-surveyed and the following table compares the survey before evacuation to that after evacuation —

TABLE III.

Summary survey

	Prior to evacuation April 1942	Subsequent to evacuation.
Total population	16 309	9 905
Total number of cases	429	209
Gross incidence	26 4	21 1
Number of open cases	60	36
Open case rate	14·0	17 1
Number of cases among children	114	57
Child rate	26 6	27·2

(*b*) This year in co-operation with the school authorities a systematic examination of all school children suspected to be suffering from leprosy has been organised. At present the scheme only embraces the Corporation schools but it is proposed to include all school children and this will give us further opportunity to study child leprosy

4 *Special Investigations at the Lady Willingdon Leprosy Sanatorium, Chingleput*

(*a*) 141 lepromatous cases were discharged in 1942 as compared to 123 in the previous year It is considered that in early cases of the lepromatous type the result of treatment is apparently good although the relapse rate is still high but that in advanced and moderately advanced cases the outlook is still very grave

(*b*) Therapeutic experiments have continued throughout the year The endeavour to discover the optimum dose of hydnocarpus oil has been continued but the results are inconclusive.

Colloidal copper is receiving a fresh trial but so far no conclusions can be drawn.

An investigation has been made of the significance of a positive Wassermann test in leprosy and of the value of Avenyl in the treatment of such cases. Two groups of seven cases were selected for this investi gation The control group received the routine treatment and the other that is the experimental group received Avenyl in pure hydno-carpus oil Patients in both groups were strongly positive to Wassermann test but had no obvious signs of syphilis. Soon after the commencement of the experiment two patients from each group dropped out leaving only five patients in each group In the control group in one case the reaction has changed to doubtful positive in 2 the reaction has become negative and in the remaining 2 the reaction

is unchanged In the experimental group one case has changed its reaction to positive, and the other 4 cases still remain strongly positive. It appears that all cases of leprosy who have a positive Wassermann reaction do not need anti-syphilitic treatment

An indigenous remedy was tried during the year without any outstanding results

(*c*) Clinical investigations were continued throughout the year, and considerable attention was given to the atypical cases, in particular to the intermediate border-line cases Much information with regard to these cases has been acquired and it appears that the majority of cases which previously were classified as tuberculoid cases in reality come under this category The true major tuberculoid is no doubt seen in South India, but it appears that the atypical tuberculoid reaction is relatively more frequent.

5 *Ettapur Childhood Rural Leprosy Control and Segregation Investigation centre*

On February 1, 1942, the Sanatorium admitted the first cases of child leprosy and thus commenced the working of the scheme which has been under contemplation for many years Thirty-seven boys were admitted during the year and 11 were discharged leaving a total of 26 at the end of the year

6 *Investigation centres at Madura, Cuddalore and Wandiwash*

The work at these centres has continued as in previous years

The Silver Jubilee Clinic at the Erskine Hospital, Madura, has become more popular because of the facilities of treating emergency cases as indoor patients

Survey work has continued in Cuddalore district though it has been handicapped as a result of widespread cholera epidemic

Owing to difficulty of starting a segregation unit at Wandiwash the work at the centre has been temporarily suspended

7 *General*

The Central Advisory Board's report on leprosy and its control in India was carefully considered and one of its important recommendations has already been implemented, the Leprosy Departments in the three Medical Colleges in the Presidency are to be reorganised and a special officer is to be placed in charge of the departments

During the year one post-graduate course was held at which 14 doctors attended

CORRESPONDENCE

CHINGLEPUT,
6th September, 1943

THE EDITOR
Leprosy in India

DEAR SIR

I was interested in reading your Editorial in *Leprosy in India* of July 1943 with regard to the question of diet and leprosy and should like the courtesy of your pages to make the following observations. The questions that need to be considered in regard to this are in my opinion four —

1. Is there any evidence that diet predisposes to leprosy?
2. Is there any evidence that diet deficiency plays any part in the development of serious leprosy?
3. Is there any evidence that on improvement of the diet better results are seen in the treatment of the disease?
4. What is the explanation of the well known fact that leprosy is most prevalent in areas where there is high carbohydrate and low protein diet?

It is generally known that we have interested ourselves in this question over the past six years. To date we have no evidence whatever that deficiency in diet is a predisposing factor in leprosy Lepromatous leprosy seems to occur in the well-nourished as frequently as it does in the under nourished, and there appears to be no relation ship between the incidence of leprosy and diet in Saidapet or in the areas where we have undertaken intensive surveys Some indigenous physicians advocate starvation as a method of treatment. In the last century arsenic was prescribed in increasing doses and this resulted in emaciation and good results were claimed. The bacilli apparently disappeared from the skin, but on return to normal health after this drastic treatment the bacilli reappeared again. All leprologists are familiar with the fact that during states of emaciation or impending death it is not an unusual phenomenon to find that bacilli have markedly diminished in the skin

The question of predisposing conditions in leprosy we believe, has been over-emphasised and it is often raised because in our ignorance we do not know why certain persons develop serious leprosy Leprosy in the lepromatous form can be described as a parasitic invasion of the reticulo-endothelial system and it appears to me that for progressive leprosy to develop the bacilli must constantly pass from internal foci in the body to the skin. This hypothesis has been suggested in the Elizabeth Matthai Lectures of the University of Madras (1943) which are to be published shortly If the skin is a necessary medium for the development of progressive leprosy may it not be a *sine qua non* that well nourished skin is a better pabulum for the multiplication of the bacilli than an under nourished one? Such a hypothesis has as much in its favour as the hypothesis that a deficient diet is a predisposing cause of leprosy

Coming to my third question we have published in the *Indian Journal of Medical Research* and in the official Indian Research Fund

Association reports the results of some of our diet experiments, and to date we can find absolutely no evidence that an improvement in diet makes the least difference to the results of treatment While, I think, the results of treatment are as good in this institution as any where else, we have still to confess that we do not know how the hydnocarpus remedies act, and we are in complete ignorance of the reason why in a certain percentage of lepromatous cases the bacilli disappear from the skin under treatment

Lastly, what is the explanation of the well-known fact that in areas of the world where there is a good all round diet the incidence of leprosy is lower than in other areas? My view I think can be summarised up as follows While diet does not appear to be a factor of outstanding importance when leprosy has once established itself in an area, but if leprosy is introduced into an area it appears probable that it is more likely to gain a footing if the diet is deficient, a poor diet may be likened to the careless match which starts a forest fire, but once the epidemic of leprosy is established the question of diet plays little or no part in its maintenance

In closing, I would make a plea to avoid what one might call 'smoke screens' in leprosy It is easy to say a patient is not getting better, because of some predisposing cause and then fold one's hands and accept such an explanation, and we even hide behind the barrier of a predisposing cause which we cannot find, or throw the blame of lack of improvement on the patient by saying that he is not taking enough exercise, or that he is worried or just that he is not co-operating, when all along the lack of improvement is due to our own ignorance of immunology, and reactions or lack of reaction of the tissue to the presence of the bacilli It is our ignorance we need to endeavour to dispel and not seek excuses for it

Yours faithfully,

(Sd) ROBERT G COCHRANE
(M.D, M R C P, D T M & H, etc.)
Chief Medical Officer,
Lady Willingdon Leprosy Sanatorium,
Chingleput, South India

[*Editor's Note* The above letter contains the views of Dr Cochrane on the editorial on 'Diet and susceptibility in leprosy' published in the July 1943 issue of this *Journal* In his concluding paragraph he makes a plea of avoiding what he calls 'smoke screens in leprosy' We do not believe that the editorial in question can in any sense be called a 'smoke screen' The relationship between diet and susceptibility to infection in general was first considered, and with this background the question of diet and susceptibility to leprosy was examined. The existing literature on the subject was reviewed, and in summing up the situation regarding diet and leprosy it was stated that 'the defective diets of countries where leprosy is common, the correlation between deficient diet and incidence of leprosy in different parts of such countries, and the reported increase in the incidence of leprosy in an area following on famines, floods, etc., are the facts which suggest a relationship between deficient diet and susceptibility to leprosy' It was clearly stated that the available evidence was only suggestive, that there was no definite evidence on this point, and that further

rk on the relationship between malnutrition and susceptibility to rosy was needed. One of our last paragraphs read as follows —

In conclusion we may say that there appears to be a definite indication on the point that in countries where leprosy is common and in persons suffering from leprosy there generally prevails a state of malnutrition and undernourishment. On general grounds one would expect this state of malnutrition to play an important rôle in predisposing to leprosy However there is no satisfactory evidence on this point since it has not been shown that the diet of persons suffering from leprosy is more deficient than that of persons living under similar conditions but not suffering from leprosy

We still stick to this view

We will now make a brief reference to the questions raised by Dr Cochrane in his letter

1 Is there any evidence that diet predisposes to leprosy? The available evidence has already been collected in the editorial in question.

2. Is there any evidence that diet deficiency plays any part in the development of serious leprosy?

There is no definite evidence on this point. However the general impression that one gets after looking at the patients in the Leprosy Department of the School is that the patients with a neural type of leprosy are on the whole better nourished than those with the lepromatous type of the disease. We do not however, mean to minimise the importance of the immunological factors which are likely to be the specific and the primary factors the diet being only a non-specific and a secondary factor

3 Is there any evidence that on improvement of diet better results are seen in the treatment of the disease?

There are workers who believe that improvement in diet does lead to better results in treatment. As a matter of fact, as Dr Cochrane himself says we do not know how hydnocarpus remedies act, it may be that they act, at least partly by improving the nutrition of the patient. At first very encouraging results in the treatment of leprosy by the addition of milk to the diet of the patients were reported by Dr Cochrane himself it appears however that on a more critical examination of the subject he has changed his views. He however still holds that wheat diet has a special place in the treatment of chronic bone and nerve pain in cases of leprosy This is certainly a case where by improving the diet better results are seen the treatment of the disease.

4. What is the explanation of the well known fact that leprosy is most prevalent in areas where there is high carbohydrate and low protein diet?

We think that Dr Cochrane's own explanation in this connection would ascribe a predisposing rôle to the diet. He says that while diet does not appear to be a factor of outstanding importance when leprosy has once established itself in an area, but if leprosy is introduced into an area it appears probable that it is more likely to gain a footing if the diet is deficient, a poor diet may be likened to the careless match which starts a forest on fire but once the epidemic of leprosy is

established the question of diet plays little or no part in its maintenance' If leprosy on introduction into an area is more likely to gain a footing if the diet is deficient, certainly it means that poor diet does play a rôle in pre-disposing to leprosy It may be that when leprosy has once established itself in a country with poor diet, the degrees of malnutrition in the different communities in a locality may not be reflected in the figures for the incidence of leprosy in these communities]

Leprosy in India

No 2 *April 1944* *Vol XVI*

EDITORIAL NOTES

Erythrocyte sedimentation test.

Erythrocyte sedimentation rate or the sedimentation index derived from it, has been widely used in various diseases. The test has been extensively used in leprosy In leprosy this test has been considered to be of great value in the detection of complicating factors such as malaria dysentery worm infections septic conditions syphilis dietetic and nutritional defects etc. in regulating the treatment with hydnocarpus oil and its preparations and in making a prognosis of the disease. It has been recommended that the test should be performed in all cases of leprosy when they come first for treatment and should be repeated once a week until the index remains steady at a satisfactory low level and then once a month or at longer intervals. In India sedimentation test is being done at most of the leprosy clinics as a routine, but it is doubtful if much useful information is being obtained, or as a matter of fact can be obtained, by the test.

In our present issue we are reprinting an article on the clinical value of blood sedimentation rate by Dr Obermer The factors involved in the erythrocyte sedimentation are not yet very clearly understood. A large number of physiological and pathological phenomenon are capable of interfering with the normal equilibrium between the red blood cells and the plasma and Obermer sounds a note of warning to the clinicians to interpret the results of the test with the greatest reserve.

The test may be of some value in acute infections Regarding its use in the chronic infections Obermer is of the opinion that variations in so sensitive a test should never be used as a reliable guide to prognosis during complex long drawn out disease processes.' These remarks he says apply particularly to a disease like pulmonary tuberculosis. However the test has been used, or rather misused, in this disease more than in any other single chronic condition. Dr Obermer's remarks regarding the use or the misuse of the test in tuberculosis should make the leprosy workers reflect on the value of the test in leprosy

Iodised hydnocarpus oil

Creosote which is usually mixed with hydnocarpus oil for injection is very difficult to get in the market We have had several enquiries from leprosy workers regarding a satisfactory substitute. In the present issue we are publishing a note on the use of iodised hydnocarpus oil. The iodised oil has been found quite satisfactory and even in fairly large doses has not produced any bad effects in the cases treated with it for over three months Simple addition of iodine to the oil will not do, the iodine should go into chemical combination with the oil and the finished product should not contain any free iodine This needs carefully heating the mixture of oil and iodine at 140°C for half an hour, and then filtering the oil

National Leprosarium, Carville

In our present issue we are reprinting an article on the recent improvements in the National Leprosarium, Carville, U S A. The article will give an idea of what is being done by the Federal Government of the States for providing comfort and all possible amenities of life to the patients of leprosy isolated in this leprosarium

The present buildings of this institution have been recently completed at a cost of about 2½ million dollars and the leprosarium at Carville can be considered the finest and the most modern in the world. There are palatial buildings for the hospital for bed patients, and for the residence of the ambulatory patients The hospital is well equipped with a first class operating room, an adequate X-ray department, a dental clinic, a bacteriological and pathological laboratory, and physio-therapy department, etc The residential buildings provide the patients with all the homely comforts, each patient has his own room with adequate modern fire-proof furniture

There are excellent arrangements for occupational therapy and for recreational facilities The recreation building completed at a cost of approximately 140,000 dollars is the most pleasing feature of the institution 'A modern motion-picture theatre, a canteen operated by patients for the benefit of the patients, smoking rooms for men and women, and a splendid library with many excellent books are on the first floor On the top floor is a huge ball or concert room with an orchestral platform on one side Here frequent dances are given by the patient body Baton Rouge and New Orleans bands come to play the latest swing music'

This will give an idea of what a country with resources can do for the comfort of those of its citizens who have to be kept in isolation. In India because of the poor resources of the country, and because of the big leprosy problem, the provision of such luxuries to the isolated persons is out of question However, it is of great importance that the State should feel the responsibility of making arrangements for the isolation and maintenance of all the infective cases, and for the maintenance of all the crippled cases of leprosy It cannot be said that in India the State has fully realised this responsibility In this connection the following quotation from the Report on Leprosy and its Control in India is thought-provoking —

> One difficulty to be overcome lies in the fact that the Central Government, provincial and local authorities have not fully realised that leprosy work is an essential part of the medical and public health work of the country or the province

and have left the work largely to private bodies. In other countries Central and local Governments have assumed direct responsibility for the work while welcoming the co-operation of and generally assisting such bodies.

Let us hope that in the post war reconstruction in the field of public health leprosy will receive the attention it deserves from the Government. It is now high time for the realisation that the control of leprosy is the inescapable responsibility of the Governments concerned.

ORIGINAL ARTICLES

THE USE OF IODISED HYDNOCARPUS OIL IN THE TREATMENT OF LEPROSY

By

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Introduction

It has been customary to add 4% creosote to hydnocarpus oil or its esters used for injection in the treatment of leprosy Due to conditions associated with war creosote has been almost unobtainable in the market In many centres plain hydnocarpus oil without the addition of any antiseptic has been used There should be no great objection to this procedure provided greater care is taken in establishing and maintaining the sterility of the hydnocarpus oil However, reports received from several centres where plain oil has been in use indicate that it has not been found a very satisfactory product for injection The oil is found more irritating than the creosoted oil and in many cases abscesses and ulcers at the site of injection have been reported. In practice this has meant a great reduction in the dose of the oil injected, and only minute doses have been used.

Efforts have been made to find a suitable substitute for creosote, and the addition of 1% thymol with oil has been found to be quite satisfactory A study has been made of the suitability of the addition of iodine to the oil for injection, and the results of this study are reported herein.

The use of Iodine in the Treatment of Leprosy

Iodine in various forms had long been in use in the treatment of leprosy, but its combination with the chaulmoogra oil was first reported by Hollman and Dean in 1916 They used a mixture of iodine, camphor, eucalyptus oil, olive oil and chaulmoogra oil for intramuscular injection (Hollman and Dean 1919) Harper (1920) used a combination of iodine, ether and chaulmoogra oil for intravenous injections When the ethyl esters were prepared from chaulmoogra oil, iodine came to be used in combination with the esters, either for injection on to the skin or by the mouth Iodine combined with the esters was first introduced in Hawaii in 1919 and later into the Philippines where it has been used since then In India the use of iodised esters has never been popular

Iodine was originally added to the esters with the idea that it might act as a curative agent and might enhance the therapeutic value of the esters After several years of experience in both Hawaii and the Philippines, it was however concluded that iodine had no such curative effect However, the addition of iodine was found to reduce considerably the irritation caused by esters It was for this

purpose that the addition of iodine to the esters has been retained for all these years.

In the beginning the proportion of iodine in the esters varied between 2 and 8 per cent. Later the addition of 2% iodine was adopted as a routine, and still later the proportion of iodine was lowered to 5% Cole (1929) stated that addition of 5% of iodine was found preferable to 2% in several respects but the reduction of iodine content to less than 5% led to the increase in the irritant properties.

While the addition of iodine to the esters has long been used, its addition to the chaulmoogra oil has not found favour Cole (1929) stated that the addition of iodine to the refined oil for reducing the irritation on injection was not necessary and that it had the disadvantage of making the oil viscid to such an extent as to make the injection extremely difficult.

The Method of Iodisation

Cole (1929) stated that it was not only the amount of iodine that was important but also the time and amount of heat used in the process. He found that heating for too long a time or to too high a temperature resulted in the production of irritating decomposing substances and that too short a period of heat or too low a tempera ture resulted in the production of a turbid greenish product which was also irritating The standard method by Cole is as follows —

Fifteen litres of purified esters are heated in 20 litres enamelled kettle at 140°C The esters must be thoroughly dried. 7½ grms. of re-sublimed iodine is added with stirring The temperature immediately rises to 150 C at which it is maintained for 30 minutes and is *stirred occasionally After cooling the iodised esters are filtered in* the bottle and sterilized for one hour in an oven at 150°C.

Our method for iodisation of hydnocarpus oil has been based on the above method of Cole for iodisation of the esters. Since we were working with the oil and with smaller quantities we had to modify the method slightly Weighed amount of pure iodine (iodine for analytical purposes) was placed in a glass mortar and was reduced to a fine powder with the help of a glass pestle. A small amount of oil was added and the grinding continued. The mixture of oil and iodine was put into a sterile dry flask, the iodine sticking to the pestle and mortar was removed with grinding with more oil which was also transferred to the flask. The flask was stoppered with a cork through which a hole had been bored for a thermometer The thermometer was put through the hole so that it dipped into the oil iodine mixture. The flask was then put in an oil bath and the temperature gradually raised. When the temperature reached 120°C. further heating was done more carefully since there is a tendency for a sudden rise in the temperature When a temperature of 140 C. is reached it is main tained for 30 minutes After that period the flask is put away for cooling When cool the iodised oil is filtered. The finished product should look brown and not greenish and when tested with starch solution it should not show the presence of free iodine.* The filtered

* The presence of free iodine is tested in the following way —A small quantity of the iodised oil is added to about a c c. of chloroform in a test tube about a c c of starch solution is added to this and the tube well shaken on

oil is put in ampoules and sterilised in an autoclave The iodised oil is not any more viscid than the plain hydnocarpus oil, and there is no difficulty in injecting this oil

A Trial of the Iodised Oil

The suitability of the iodised oil for injection has been tested in 20 cases of leprosy, 10 of each type At the time of writing of this note, these cases have been receiving this treatment for about three months All these cases had been under treatment at the Leprosy Department and were receiving injections of creosoted hydnocarpus oil previous to the injections of the iodised oil.

The iodised oil has been injected into these patients by all the three methods, subcutaneous, intramuscular and intradermal In the beginning the injections were given twice a week, and the patient received both the iodised and the plain or creosoted oil. Later the injections were given only once a week and only the iodised oil was used

The iodised oil has been given in fairly large amounts The initial dose in most cases was 2 c c. This dose was gradually increased, and all the cases except one have now been receiving doses of more than 5 c c, and some even more than 10 c c. The total number of injections have been 10 or more in 11 cases, and between 5 and 10 in 9 cases

The object of this trial has been to get information on the following points in connection with the iodised oil —

1 Pain at the time of injection and later
2 The induration at the point of injection.
3 A tendency to formation of an abscess or ulcer, etc
4. A tendency to produce lepra reaction
5 Hyper-pigmentation produced at the site of injection

The Results of the Trial

Pain at the time of injection —The intradermal injections of iodised oil on the whole cause the same amount of pain as those of plain oil The intradermal injections of iodised oil cause a little more pain than those of creosoted oil

Intramuscular and subcutaneous injections of the iodised oil do not cause any pain.

Induration —The intradermal injections of iodised oil cause more induration than those of the plain or the creosoted oil. This greater induration does not last for very long

Abscess or ulcer at the site of injection —No abscess or ulcer has been seen after the intradermal, intramuscular or subcutaneous injections of the iodised oil.

Hyperpigmentation at the site of injection —The iodised oil causes slight hyperpigmentation at the site of intradermal injections

Signs of reaction —Since potassium iodide is known to bring about lepra reaction in several cases of leprosy, a special note was made of any symptoms suggesting the occurrence of reaction after

standing the mixture separates into two layers chloroform with the dissolved oil at the bottom and starch solution at top and in the presence of free iodine in the oil, a blue colour appears in the starch solution

injections of the iodised oil On each day of attendance enquiries were made from the patients whether they had experienced any rise of temperature after the previous injection or whether there had been any thickening and reddening of the lesions or appearance of any new lesions. In addition the patient's body was carefully examined for any thickening or reddening of the lesions, and for the appearance of new lesions.

Of the 10 neural cases 3 reported a slight rise of temperature once on the day of injection or on the following day In another case an area with an erythematous border was noticed near the point of an intramuscular injection, this area later disappeared

Of the 10 lepromatous cases 6 reported a rise of temperature more than once on the day of injection or on the following day One of these patients reported slight exacerbation of the lesions on the face after one or two injections but this increase was not visible and the complaint of the patient did not persist.

Many of the cases both lepromatous and neural complained of itching either in only the injected part or over the whole body

Thus in the neural cases there was nothing much suggestive of reaction In the lepromatous cases a rise of temperature was seen oftener but even in these cases nothing serious was noted.

Antiseptic Value of the added Iodine

The above observations showed that iodised oil is on the whole quite suitable for use in patients of leprosy but they do not indicate whether the iodised oil possesses an advantage over the plain oil. Since one of the complaints against the plain oil is that it gives rise to abscesses ulcers etc. attempts were made to find out if the added iodine had any antiseptic value and would thus reduce the incidence of abscesses etc. Cultures of staphylococcus aureus were added to samples of sterilized plain and iodised oils in test tubes. These oils were incubated at 37°C. and subcultures from the two specimens of the oil were made after 24, 48 72 and 96 hours. The oil itself is not a very good medium for the multiplication of the pathogenic organisms, and our experiment did not give very clear-cut results. However, the results obtained suggested that the added iodine had some antiseptic value, since the number of colonies of staphylococci growing in subcultures from the plain oil were more than such colonies growing from the iodised oil

Conclusions

The iodised oil appears to be quite suitable for injection into cases of leprosy Moreover the added iodine appears to have some antiseptic action It is proposed that the iodised oil may with advantage be used in place of the plain oil

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INTRADERMAL TESTS WITH ANTIGENS PREPARED FROM THE URINE OF CASES OF LEPROSY

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Introduction

Berny and Mauze (1940) described an intradermal reaction in cases of leprosy, which they considered to be of diagnostic value They used an antigen prepared from the urine of bacteriologically positive cases of leprosy, and reported to have obtained 100% positive results in cases of leprosy, and none in controls If confirmed, this test would be of great value, since no other diagnostic skin test for leprosy is available at present, the lepromin test, the only immunological skin test of value in leprosy, has no diagnostic value, since it gives positive results in only one type of cases, the neural cases, and negative results in the other and the more serious type, the lepromatous cases, and since it gives positive results in many non-cases The antigen used by Berny and Mauze is supposed to have given positive results in all the cases of leprosy of both the types, and negative results in non-cases An attempt has been made to confirm this work, and the results are reported herein

The Work of Berny and Mauze

Berny and Mauze prepared the antigen from the urine of eight bacteriologically positive cases of leprosy To the mixed sample of fresh urine, free from albumen, they added three times the volume of 95% alcohol This resulted in the formation of a precipitate The mixture was allowed to stand for 24 hours after which the supernatant fluid was decanted and the precipitate was centrifuged and dried in vacuum A 3% solution of this dry extract was made in normal saline, and the solution was filtered. To 200 c c of this filtrate 10 drops of ammonia were added, the mixture was filtered and the *p*H of the filtrate was adjusted between 6 4 and 6 6 with acetic acid This was then put into ampoules and preserved in an ice box. For the test, 2 to 3 drops of this extract were injected into the skin of one arm, and an equal amount of distilled water as a control in the other arm

This extract was tested in 199 cases of leprosy in all stages, in 5 suspects, and in 91 healthy subjects, and observations were made after 8, 24 and 48 hours In cases of leprosy there was a rise of temperature to 38 or 39 degrees centigrade in 8 hours, and after 24 hours a papule exceeding 2 cm in diameter appeared, usually accompanied by erythema and pain Such reactions are reported to have been obtained in all the cases of leprosy and in none of the controls.

The present work

Antigen prepared from bacteriologically positive lepromatous cases of leprosy not in the stage of reaction —Antigen was prepared from albumen-free samples of urine of bacteriologically positive cases of

leprosy according to the method of Berny and Mauze. The only difference was that the strength of the final solution of the dry extract was 2% in place of the 3% used by these workers. This modification was necessitated by the fact that the dry extract is sparingly soluble in saline. Chemical tests made on the final solution showed that the substance was of the nature of secondary proteoses, it gave a positive Biuret reaction and a precipitate with copper sulphate and ammonium sulphate but no precipitate with nitric acid

In addition to the above antigen the following three preparations were used for comparative tests in the same patient —

1 Proteoses from urine of healthy persons not suffering from leprosy
2 A solution of proteoses obtained from Witte s peptone This solution was given all the treatment used in the preparation of proteoses from urine that is ammonia was first added to the solution it was then filtered and the *p*H of the filtrate was adjusted to 6 8
3. A solution of a protein fraction of the Hansen's bacillus.

The Results —The above four preparations were tested in cases of leprosy of both the types about two dozen each and the patients were examined for reaction at the site of injection 24 hours after injection.

The lepromin test with the protein fraction of the Hansen s bacillus produced the usual results that is reactions of the tuberculin type in the neural cases and no reactions in the lepromatous cases.

The proteoses from the urines of both the healthy persons and the bacteriologically positive cases of leprosy produced no reactions either in the lepromatous or the neural cases

The proteoses from Witte s peptone produced extensive erythema and some induration at the site of injection in all the cases both the lepromatous and the neural. The reaction to this preparation appeared to be more of inflammatory nature than of allergic nature.

The results obtained in cases of the two types with these different preparations are summarised in the following table —

	Protein fraction of Hansen s bacillus (lepromin test)	Proteoses from healthy urine	Proteoses from urine of bacteriologically positive cases of leprosy	Proteoses from Witte s peptone
Lepromatous	—	—	—	Extensive erythema and some induration
Neural	+	—	—	Extensive erythema and some induration

Antigen prepared from a bacteriologically positive lepromatous case in the stage of reaction.—In view of the negative results obtained with

the proteoses from non-reacting bacteriologically positive cases of leprosy, the urine from reacting cases of leprosy was next used in the hope that positive results may be obtained from such specimens The extract was prepared in exactly the same method as used for the urine from the non-reacting cases

The Results —This antigen was tried in one and a half-dozen lepromatous cases, and half a dozen neural cases It produced reactions in all the neural cases, and in several of the lepromatous cases The reaction produced was not the typical tuberculin type of reaction, but was more of the inflammatory type

In view of the nature of the reaction produced it was considered that the reaction was the result of injury and irritation to the skin tissue, and that the *p*H of the solution used might have contributed to the reaction seen The solution of this antigen was therefore made in saline of two different *p*H, 6 8 (acid) and 7 8 (alkali) These two solutions were tested in the same persons It was observed that the reaction was appreciably less marked with the solution at *p*H 7 8 than with the one at *p*H 6 8 This difference was specially marked in cases of the lepromatous type

A comparison of antigens obtained from non-reacting and reacting lepromatous cases —The above results with the antigens prepared from the urine of a lepromatous case of leprosy in the stage of reaction appeared hopeful It was considered possible that the urine of the reacting cases of lepromatous leprosy contained some substance which is not found in the non-reacting cases of this type, and which may be found to be of value for the purpose of a diagnostic skin test in leprosy With this point in view antigens were prepared from two bacteriologically positive lepromatous cases, one of whom was in the stage of reaction These two antigens were tested in cases of leprosy of the two types, on a dozen of each type. The results obtained did not substantiate the hopes aroused by the preceding results In none of the lepromatous cases either of the antigens produced a positive result In the neural cases both the antigens produced positive results in only two cases and negative results in the remaining ten The result showed that in this instance the antigen prepared from the non-reacting case did not differ from the one prepared from the reacting case, and that the urine of the reacting case did not contain an antigen which could be utilised for a diagnostic skin test in leprosy

Conclusion —Extracts made according to the method of Berny and Mauze from the urine of non-reacting bacteriologically positive cases of leprosy have failed to produce any skin reaction in all the lepromatous and most of the neural cases tested. A similar preparation from a case of lepromatous leprosy in the stage of reaction produced skin reaction in the neural and several of the lepromatous cases tested. However, these results were not constant since the extract from urine of another reacting lepromatous case failed to produce reactions in any of the lepromatous cases and many of the neural cases tested. The intradermal reaction described by Berny and Mauze cannot therefore be used as a diagnostic skin test for leprosy

Summary

1 A description is given of the intradermal reaction of Berny and Mauze in cases of leprosy with extracts prepared from the urine of bacteriologically positive cases of leprosy

2 Extracts prepared according to the method of Berny and Mauze from non reacting bacteriologically positive cases of leprosy have not produced any reaction in all the lepromatous and most of the neural cases tested Extract from the urine of one lepromatous case in the stage of reaction produced positive results in the neural and several of the lepromatous cases tested This however was not a constant feature since extract prepared from another reacting case produced reactions in only a few of the neural and none of the lepromatous cases tested.

3. The extract prepared from the urine appears to be of proteose nature. The positive results obtained with this extract were similar to, though weaker than, the results produced by proteoses obtained from sources unconnected with leprosy

4. The results obtained do not confirm the statement of Berny and Mauze that the antigen from the urine of bacteriologically positive cases of leprosy can be used as a diagnostic skin reaction for leprosy

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REPRINTED ARTICLES

RECENT IMPROVEMENTS IN THE NATIONAL LEPROSARIUM CARVILLE, LA

(From International Journal of Leprosy, Vol 10, Dec 1942, page 140)

Until recently most of the buildings of the Federal Leprosari at Carville were of wooden frame structure and therefore a fire haza Starting in the spring of 1940, at a cost of approximately two and h million dollars, the Government undertook to rebuild the institut almost completely, in order to make it fireproof This build program was completed by the end of 1941 Facilities have b increased to take care of 480 ambulatory patients, in addition to 65 hospital rooms for bed patients At present the leprosarium Carville can be considered the finest and most modern in the world

The visitor who approaches the Federal Leprosarium at Carv for the first time is surprised to see such imposing buildings in otherwise rural district After he enters the reservation of 350 ac he is impressed by the fact that it is a self-sustaining communi resembling a small town There is a power plant for the generat of electricity, the manufacture of ice, and the operation of a stea radiator heating system. A modern sand filtration plant with attach chlorinating apparatus furnishes over 200,000 gallons of pota water a day Both hot and cold water is piped to all the buildi of the colony The water consumption per capita is above that most large cities in the United States This meets with the appro of the administrative force, since cleanliness is conducive to hea and the source of supply, the Mississippi River, is inexhaustib There are two modern sanitary laundries, one for the patients, t other for the personnel A large sanitary dairy with pasteurizati and cold storage facilities produces 180 gallons of Grade A m a day Cattle are raised to furnish beef products Protestant a Catholic churches and their respective resident chaplains afford t patients religious comfort A well-equipped fire department is rea to function at all hours The sewage system with its septic tan and the incinerator plant for the disposal of garbage assure the co plete sanitation of the community and protection of the neighbouri public. An extensive drainage system demands constant attenti to prevent a mosquito nuisance and a possible malaria menace. I sides the numerous buildings for the use of the patients and the lar nurses' home, there are 25 residences for doctors, administrati clerical, mechanical, and other employees All the personnel a employees of the Federal Government, there are no volunteer worke Paved roads connect the different parts of the reservation.

Passing from the personnel to the colony side of the estate, t visitor comes first to the hospital where the bed patients are treate This is a two-story concrete building containing 44 rooms for men a 21 rooms for women patients In addition, it contains a first cla operating room, an adequate X-ray department, a dental clinic, bacteriologic and pathologic laboratory, a physio-therapy departmer dressing-room clinics for men and women, offices and examining room

The ambulatory patients who are by far in the majority are domiciled in 16 two-story concrete buildings. Each of these buildings contains on each floor, 15 individual bedrooms bathrooms, a reception room and front and back porches. The front porches are connected upstairs and downstairs by concrete passage ways screened and covered for the protection of the patients in going about the colony

Every effort has been made to provide the patients with the comforts of home for the most part they are contented and well satisfied with all that is being done for them. They can pursue their avocations and enjoy a variety of community activities. Each patient has his own room with adequate modern fireproof furniture. He may arrange and decorate his room to suit his taste. Visitors are allowed as in other hospitals There are no restrictions in correspondence with relatives or friends except that all outgoing mail is disinfected.

On each side of the hospital is a building for occupational therapy Each of these two-story buildings has 18 rooms These are used as sewing room, music room school room photography room barber shop tailor shop pressing shop carpenter shop shoemaker's shop bicycle repair shop radio repair shop rooms for various other arts and crafts and finally the printing offices of the patients local paper *The Star* This is an interesting monthly periodical the purpose of which is radiating the light of truth on Hansen s disease It contains many splendid articles from the pens of patients Its outside circulation is increasing Occupational therapy in its different forms is a useful part of the patients treatment. Occupation has a good moral effect upon the patient it prevents brooding upon his malady The employment of 98 patients on a small salary basis by the Government serves the same purpose It also affords them ready cash for the purchase of the little luxuries not furnished by the Government. The Government provides all patients with food, clothing, toilet articles books, magazines newspapers a golf course, tennis courts baseballs basketballs, and other sporting equipment and three motion-picture shows each week.

The new recreation building has filled a long felt need at the National Leprosarium. This beautiful, spacious two-story structure is the feature of the new construction program which has pleased the patients most. It cost approximately $140 000 and was well worth the price for the recreational facilities it affords this group of shut in citizens from practically every State of the Union. A modern motion-picture theatre, a canteen operated by patients for the benefit of the patients smoking rooms for men and women, and a splendid library with many excellent books are on the first floor On the top floor is a huge ball or concert room with an orchestral platform on one side. Here frequent dances are given by the patient body Baton Rouge and New Orleans bands come to play the latest swing music.

The patients are served their meals cafeteria style at 7 a.m. noon, and 5 p.m. The dining room adjoins a clean well-equipped kitchen. Menus are carefully planned the food is well cooked, tasty and nutritious The meals served can be compared to those of a first class hotel. Food plays a direct part in the fight against the disease and no effort is spared to provide the best.

column of blood has been pushed half-way up, the capillary tube should be reversed, the column of blood run to the other end, and this end inserted into the drop of blood until the whole length of the tube is filled

The ball of plasticine is then held in the left hand, the blood filled tube, horizontally, in the right hand, and the left end of the tube is inserted into the plasticine for a depth of 4 mm. This can be verified by measuring the length of the projecting tube, it should measure exactly 10 mm.

The tube is then placed vertically in the incubator, or dropped into the test tube in the waistcoat pocket Readings of the supernatant plasma are taken at the end of fifteen, thirty and sixty minutes

The upper limits of normality by this method are —

15 minutes	up to 0 4 cm	(4 mm)
30 ,,	,, 1 0 cm	(10 mm)
60 ,,	,, 2 5 cm.	(25 mm.)

When red blood cell figures are available, no correction need be made unless the count is below 4 millions or over 5½ millions Above or below these limits, the reading should be multiplied by the factor R B C *in millions*

WHAT THE TEST MEANS

This is not the place to discuss the highly technical factors involved in the mechanism of erythrocyte sedimentation, even experts do not agree on this subject Readers are referred to Balachowsky (1925) for intrinsic red cell factors, to Bendien and Snapper (1931) for the plasma protein factor (the authors prove that there is a direct correlation between fibrinogen content and sedimentation rate) and to Rossier (1927) for physico-chemical details The last named author showed a parallelism between curves of sedimentation rate and isoelectric points of the plasma The following facts, however, are well established —

(*a*) The sedimentation rate is surprisingly constant for the individual under physiological conditions

(*b*) *In vivo*, or at body temperature, the normal equilibrium between red blood cells and plasma is ruptured by a large number of physiological as well as pathological phenomena. Thus the absorption into the blood stream of minute quantities of foreign protein, colloidal metals and a number of other substances is sufficient to increase the sedimentation rate to a significant extent

(*c*) Extravasated blood from a simple bruise or from the uterine cavity during menstruation, placental proteins, and even absorption of cells, destroyed as part of the ordinary wear and tear of the tissues (when katabolism is accelerated) may influence the rate to an even greater degree It is therefore important for the clinician to realise that the results of this test must be interpreted with the greatest reserve From the diagnostic point of view, abnormal figures, i e. an increased rate, have relatively little value unless correlated with many other data. More reliance, however, may be placed on normal figures Even so, it must be stressed that normal

figures mean, simply that no absorption of abnormal products is taking place.

It is reasonably safe to assume that the presence of an inflammatory process is incompatible with sedimentation rate figures which are within normal limits. There are however, rare exceptions to this rule. A few people for reasons which are not yet understood have an extraordinary slow sedimentation rate.

In one case in my series (a young man of thirty) serial determinations were done over a period of two to three years In health his rate never varied i.e. 0 0 at fifteen minutes 0·2 at thirty minutes, 0·5 at sixty minutes. Throughout an acute pyrexial attack of tonsillitis during which daily determinations were made the rate remained within normal limits.

The rate is also abnormally slow in the presence of polycythaemia at high altitudes and in persons of a plethoric habitus

Finally the clinician should remember that increased plasma volume, due to anaemia causes an increased rate of sedimentation When a red blood cell count is possible, a correction can be made. In its absence, if the clinician suspects anaemia he cannot attach any importance to an increased rate. For further details on this point readers are referred to Walton (1933) and Schuster (1938)

Diagnostic value of Pathological Variations

Explanatory—From what has been said it will be seen that many pathological processes within the body cause a marked increase in the sedimentation rate, owing to the fact that normal cells when damaged, function as foreign protein. An increased rate may therefore be caused by blood extravasated through injury or operative interference by transudates or exudates by autolytic or necrotic tissue changes as in malignant neoplasms syphilitic gummas and also by caseation and fibrinoplastic changes

It is also true that the rate is increased when the body is reacting to an inflammatory process The degree of increase tends to be proportional to the severity of the infection Such an increase is almost certainly due to the inflammatory reaction or rather the absorption of the products of such a reaction. Thus the rate is very rapid in osteomyelitis and in acute furunculosis but is not increased in the presence of a cold abscess It may be assumed that the latter is due to the fact that the pus in a cold' abscess is completely walled round' and that there is no systemic absorption from the pus sac.

By the same rationale it is legitimate to use the sedimentation figures as a rough estimate of the degree of systemic toxic absorption in a number of conditions. Thus if the rate is normal when dental skiagrams show an apical abscess the clinicians may be justified in asking the dentist to spare the tooth the abscess is probably walled round and is not doing the patient any harm It is as yet, a moot point whether or not the absorption of bacterial toxins alone can cause an increase in the rate.

In miscellaneous conditions (*a*) *The abdominal case*—A negative test at the bedside in an acute abdomen may help the clinician to differentiate between simple colic and appendicitis or other

inflammatory process within the abdomen The same applies t acidotic vomiting in children and the differentiation of an allergic colit from an infective one

(*b*) *Functional cases*—An increased rate may be found o examining individuals complaining of symptoms without any detec able physical signs In such cases it is often justifiable to incriminat focal sepsis

(*c*) *Rheumatism*—This test can be of some small assistance in th blind groupings through this diagnostic 'no man's land', but it shoul never be used as a 'compass' The factors involved are far too com plicated to permit anyone, however skilled, to use sedimentatio figures as a guide to prognosis or treatment In well-defined path logical joint states, such as rheumatoid arthritis, that rate is invariabl increased, but variations in the clinical conditions are a more reliab guide to progress than the sedimentation rate When there is nerv or muscle pain, a negative test is of some value, as the clinician ca then, tentatively, exclude active focal sepsis

Acute and subacute infections—In mild infections, such as coryz an increase in the sedimentation rate is usually proportional to th degree of systemic disturbance If tracheitis or bronchitis supe vene, the rate of sedimentation is often a better guide than the tem perature curve Similarly, in the subacute phase of influenza, otit media, pelvic or urinary tract infections, an increase, instead of decrease, in the rate may put the clinician on his guard against com plications A maximum increase in the rate is found (*a*) during th acute phase of the common fevers, in particular scarlet fever, i which the fibrinogen content of the blood is very high, and (*b*) in lob pneumonia, owing to the double effect of toxic absorption and resor tion of the pulmonary exudate

Chronic infections—Enough has already been said to show th variations in so sensitive a test should never be used as a reliab guide to prognosis during complex, long-drawn-out disease processe This applies particularly to a protean disease, such as pulmonar tuberculosis It is true, however, that the test has been used, c rather misused, in this disease more than in any other single clinic condition Variations in the sedimentation rate and in 'sedimentatio index' (an ingenious mathematical abstraction—unfortunately wo shipped by its devotees as an infallible prognostic deity) have bee interpreted with the most unjustifiable dogmatism. As secondar infection is extremely common in chronic pulmonary tuberculosi and as autolytic and reparative changes in the lung continue even in quiescent or arrested case, the accurate interpretation of sediment tion changes in tuberculosis is well nigh impossible In fact, it ma be said that an increased rate of sedimentation in pulmonary tube culosis can be considered of clinical significance only when it is corre lated with all the clinical and radiological data, and with simultaneou determinations of plasma protein content (by an accurate chemica method), plasma viscosity, refractive index of the plasma (permittin a rough estimate of the albumin globulin ratio) and a complete bloo count, including a Schilling or Arneth differentiation of the poly morphonuclear cells As facilities for such a complete investigatio are rarely available in sanatorium or dispensary practice, the test is o doubtful utility in this condition

Limitations and Contraindication

The test cannot be relied upon in the following circumstances —

(1) *Infancy* —During the first few months of life, the red blood cells do not sediment no satisfactory explanation has as yet been put forward.

(2) *During menstruation* —Some women consistently show an increase in the rate during the flow In others the rate remains normal Here again, no explanation has been put forward It is to be hoped that the mechanism of this phenomenon will be worked out as it may throw light on several obscure pelvic problems From a practical point of view however it is wiser not to perform the test on women during the menses

(3) *Pregnancy* —From about the twelfth week of pregnancy to the fourth week post partum, the rate is invariably increased

(4) *After accidental or operative trauma* —Until healing or cicatrization has occurred

(5) *Hypodermic treatment* —Subcutaneous or intramuscular injections of vaccines peptone, casein, or other foreign proteins colloidal metals and autohaemotherapy

Conclusions.

The sedimentation rate of the blood reflects static phases of a delicate and unstable equilibrium This equilibrium is destroyed or disturbed by the absorption into the blood stream of a number of substances of which inflammatory products are only one. So sensitive a test is undoubtedly capable of yielding information of the greatest value to the clinician However much of this information cannot yet be interpreted with accuracy because different workers have used different methods and have not adequately correlated the sedimentation figures with other blood findings and clinical data The way forward to a clearer understanding of the value of this test is twofold —

(1) Through the routine use of a standardised test by a large number of practitioners in their surgeries and at the bedside.

(2) The wider use of laboratory facilities in hospitals sanatoria and research institutes for more comprehensive blood work including a determination of the sedimentation rate by the same standardised method.

Only thus can a new literature on the sedimentation rate of practical as well as theoretical value be established to replace the present confusing record of dissociated and uncorrelated data.

Summary

(1) The theoretical and practical requirements of an ideal method for determining the blood sedimentation rate are given.

(2) A simple method for estimating the sedimentation rate in the laboratory or at the bedside is described.

inflammatory process within the abdomen. The same applies to acidotic vomiting in children and the differentiation of an allergic colitis from an infective one

(*b*) *Functional cases*—An increased rate may be found on examining individuals complaining of symptoms without any detectable physical signs In such cases it is often justifiable to incriminate focal sepsis

(*c*) *Rheumatism*—This test can be of some small assistance in the blind groupings through this diagnostic 'no man's land', but it should never be used as a 'compass' The factors involved are far too complicated to permit anyone, however skilled, to use sedimentation figures as a guide to prognosis or treatment In well-defined pathological joint states, such as rheumatoid arthritis, that rate is invariably increased, but variations in the clinical conditions are a more reliable guide to progress than the sedimentation rate When there is nerve or muscle pain, a negative test is of some value, as the clinician can then, tentatively, exclude active focal sepsis

Acute and subacute infections—In mild infections, such as coryza, an increase in the sedimentation rate is usually proportional to the degree of systemic disturbance If tracheitis or bronchitis supervene, the rate of sedimentation is often a better guide than the temperature curve Similarly, in the subacute phase of influenza, otitis media, pelvic or urinary tract infections, an increase, instead of a decrease, in the rate may put the clinician on his guard against complications A maximum increase in the rate is found (*a*) during the acute phase of the common fevers, in particular scarlet fever, in which the fibrinogen content of the blood is very high, and (*b*) in lobar pneumonia, owing to the double effect of toxic absorption and resorption of the pulmonary exudate

Chronic infections—Enough has already been said to show that variations in so sensitive a test should never be used as a reliable guide to prognosis during complex, long-drawn-out disease processes This applies particularly to a protean disease, such as pulmonary tuberculosis It is true, however, that the test has been used, or rather misused, in this disease more than in any other single clinical condition Variations in the sedimentation rate and in 'sedimentation index' (an ingenious mathematical abstraction—unfortunately worshipped by its devotees as an infallible prognostic deity) have been interpreted with the most unjustifiable dogmatism As secondary infection is extremely common in chronic pulmonary tuberculosis, and as autolytic and reparative changes in the lung continue even in a quiescent or arrested case, the accurate interpretation of sedimentation changes in tuberculosis is well nigh impossible In fact, it may be said that an increased rate of sedimentation in pulmonary tuberculosis can be considered of clinical significance only when it is correlated with all the clinical and radiological data, and with simultaneous determinations of plasma protein content (by an accurate chemical method), plasma viscosity, refractive index of the plasma (permitting a rough estimate of the albumin globulin ratio) and a complete blood count, including a Schilling or Arneth differentiation of the polymorphonuclear cells As facilities for such a complete investigation are rarely available in sanatorium or dispensary practice, the test is of doubtful utility in this condition

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Summary

(1) The theoretical and practical requirements of an ideal method for determining the blood sedimentation rate are given.

(2) A simple method for estimating the sedimentation rate in the laboratory or at the bedside is described.

(3) The mechanism of sedimentation is discussed

(4) An explanation is given for variations of the rate in physiological and pathological conditions

(5) The diagnostic value of the test in various conditions, including infective and inflammatory processes, is subjected to a critical review

(6) Stress is laid on the value of normal figures (a negative test), and upon the necessity for extreme caution in interpreting abnormal figures

(7) A list is given of the conditions which contraindicate the use of the test

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ABSTRACTS FROM CURRENT LITERATURE

International Journal of Leprosy Vol. 10 December 1942

This issue of the *International Journal of Leprosy* is a special War Number The publication of the journal had to be suspended due to conditions associated with the war in the Pacific. With a view to maintaining as far as possible the continuity of leprosy work the American Leprosy Foundation (the Leonard Wood Memorial) has decided to bring out from time to time special war numbers of the journal In the Foreword Mr Perry Burgess President of the Leonard Wood Memorial dedicates this number to the editor Dr H. Windsor Wade and to all workers in leprosy physicians laymen and their families who have been interned at their posts. This number is edited by Dr James A Doull of the Western Reserve University Cleveland

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Original Articles

Reprinted Articles

Saunders article gives a general description of the Virgin Islands a historical sketch and an account of the general medical condition in the island The prevalence of leprosy in the island is then discussed

The Virgin Islands of the United States lie in the Lesser Antilles part of that curving crescent of the West Indies which bounds the Caribbean Sea on the north and east They are situated about 40 miles east of Puerto Rico, and 1,400 miles south of New York There are more than 50 islands and Cays in the group but only three are of any size or importance These are St Croix, St Thomas and St John, which include practically all of the land area of 133 square miles, and of the population of 25,000 St Thomas and St John lie close together near the British Virgin Islands, while St Croix is 40 miles to the south in the Caribbean

The data on which the study of the prevalence of leprosy is based were obtained from several different sources, namely the official Danish and unofficial church burial records, the leprosarium records, personal communications, and the leprosy survey of 1938-1940 The records from 1841 to 1930 show a total of 930 cases of leprosy (of whom 147 are still living) but the author believes that this figure is an under-estimate The vast majority of recorded cases were diagnosed in St Croix, and in this island the incidence of the disease has been much higher than in the other islands

Of the total cases recorded (930) 499 have been males and 431 females For the 60-year period (1841 to 1899) the gross leprosy attack rate was 18 9 per 1,000 males, and 13 7 per 1,000 females For the 40-year period from 1900 to 1939 the male rate was 15 6 per 1,000 and the female rate 13 7 per 1,000 Considering only the cases living in 1940 the prevalence per 1,000 is found to be 4 9 for males and 5 2 for females In other words there seems to have been a shift from the higher male incidence to a higher female incidence The author, however, considers that the male preponderance before 1910 may be more apparent than real since the conditions in the leprosarium up to 1910 were so bad that females might have objected more than males to being isolated, before 1910 more males were admitted than females, but since 1910 there have been 89 male and 92 female admissions

The incidence of leprosy has declined in these islands and the decline has been more rapid during the past 30 years Probably two significant factors have been associated with this decline during this period, viz (1) the elevation of the social and economic level has led to a general decrease in mortality and morbidity in which leprosy has shared, and (2) the isolation of cases of leprosy which began at 1888 was very incomplete until 1910 but has been fairly complete since then

The 1939/1940 leprosy survey revealed a total of 127 definite cases and 20 persons with suspicious signs of leprosy If only the 127 definite cases are taken into account, the incidence of the disease works out at 5 1 per 1,000 for the Virgin Islands as a whole, 8 6 per 1,000 for St Croix and 1 5 per 1,000 for St Thomas

The author concludes the article as under —

(1) Leprosy has been present in the Virgin Islands for at least 100 years
(2) Incidence has diminished since 1841 and the decline has probably been more rapid during the past 30 years
(3) The average age at death for persons with leprosy has increased steadily during the past century, males dying considerably earlier than females The average age at death for the whole population has run parallel to that for persons with leprosy, but at a higher level

(4) At the present time the highest prevalence is found in St. Croix with more than 8 cases per 1 000 next highest in St Thomas with about 1 5 cases per 1 000 and no cases are known in St John.
(5) At present there is a slightly greater prevalence in females than in males although formerly the reverse seems to have been true

Saunders and Guinto report on a leprosy survey carried out in the Virgin Islands in 1939 and 1940 A complete census of the population on the island was taken and about 70% of the population in one of the islands and about 95% in the other island were carefully examined The authors summarise their findings as under —

1 A field study of leprosy in the Virgin Islands has demonstrated that the disease is about ten times as prevalent in St. Croix (10–14 per 1 000) as in St. Thomas (1–1 5 per 1 000) and previous reports indicate that for at least 100 years the relative frequency has been much the same St. Thomas has been favoured economically its people have a more adequate diet it has had a higher level of health and sanitation, and it has had considerably lower general mortality and morbidity rates than St Croix

2 In two-thirds of the cases of leprosy the first signs of disease appeared before 20 years of age a smaller proportion than in Cebu, Philippine Islands. It is suggested that the greater prevalence in Cebu may favour earlier infection.

3 Prevalence in the Virgin Islands increases with age and it is greater in persons over 50 years old than in most other localities where intensive surveys have been made The large proportion of cases in older age groups is interpreted as suggestive evidence of declining incidence

4. Leprosy is about equally prevalent in females and males in the Virgin Islands a condition similar to that found in West African natives but in marked contrast to that found in the Philippines and most other areas. If males are more susceptible to the disease they would be expected to exhibit higher prevalence universally and not in certain localities only It is suggested therefore that in the Philippines males may be more exposed than females whereas in the Virgin Islands exposure may be approximately equal It should be borne in mind, however that even where infections are equally common in females and in males, a greater proportion may conceivably remain latent in one sex than in the other because of some environmental variation.

5 Leprosy was found to be more prevalent in Negroes than in other racial groups in the Virgin Islands.

6 A history of contact with antecedent cases, either within or without the household was obtained in nearly 70 per cent of patients under 20 years of age but in a much smaller proportion of older cases.

7 Leprosy was found to be much more frequent among the lower economic classes where there are found also higher morbidity rates for other diseases less cleanliness less favourable housing conditions and a more inadequate diet

8 Lepromatous leprosy comprises less than 30 per cent and neural leprosy more than 70 per cent of all cases in the Virgin Islands. These proportions were found to be essentially the same in males as in females

Saunders and Giffen report on the histological findings in the skin lesions in 30 cases of leprosy in the Virgin Islands. The clinical and histological features of these lesions were similar to those seen elsewhere in such cases. Clinically the majority of the lesions were pale and flat macules with at least a portion of the periphery granular or papular in only one case were the lesions raised indurated and swollen (major tuberculoid) The lesions in all cases were bacteriologically negative Sensory changes were found in one or more lesions in practically all cases In 7 cases the histological examination showed banal subacute or chronic inflammation with infiltration with lymphocytes and histiocytes In the remaining 23 cases the granuloma was of the tuberculoid type, that is an aggregation of epithelioid cells usually occurring in discreet foci with or without giant cells surrounded by moderate numbers of lymphocytes or other cells of chronic inflammation. Small nerve fibres of the corium were commonly involved in the granulation process

Kean and Childress report on the autopsy findings in 103 cases of leprosy on the Isthmus of Panama They summarise their article as under —

1 Of 103 autopsies performed on lepers at the Board of Health Laboratory Gorgas Hospital, Ancon Canal Zone between the years 1904–1941, 79 were on males and 24 on females Although half of the patients were found in the cities of Panama and Colon, the evidence suggests that many cases were imported from Jamaica and Barbados Foci of leprosy probably exist in the provinces of Los Santos and Bocas del Toro

2 The average age of recorded onset of leprosy was 36·7 years, the average age of death was 47 1 The most frequent 'first symptoms were nodules of the face and ulcers of the feet

3 The pathologic changes in all the organs were listed systematically Some of the findings worthy of comment are

(*a*) Leprosy affected the nasopharynx or upper or outer portion of the upper respiratory system, whereas tuberculosis affected the larynx and trachea or lower portion of the upper respiratory system

(*b*) A high incidence of cirrhosis of the liver

(*c*) A high incidence of gallstones

(*d*) A high incidence of nephritis especially glomerulonephritis

4 The final causes of death were, in the order of numerical importance, tuberculosis nephritis leprosy and heart disease

Doull and Bryan report on the amount of diphtheria anti-toxin in 22 cases of leprosy in Puerto Rico This investigation was undertaken to find out whether there is any scientific basis for the use of diphtheria anti-toxin in the treatment of leprosy since the use of diphtheria toxoid in cases of leprosy should imply that in leprosy natural anti-toxin is deficient or lacking The results of the study showed that leprosy patients in Puerto Rico have as a rule substantial quantities of diphtheria anti-toxin in their blood

Schujman and Mercau report on the treatment of leprosy with diphtheria toxoid They included 11 patients in their study, 10 of the lepromatous type and 1 of the tuberculoid type. Diphtheria toxoid was injected intramuscularly commencing with 1 c c and increasing rapidly to a dose of 3 c c which was repeated weekly All the 11 patients were treated for approximately five months, and each received from 15 to 17 injections (a total of 45–50 c c of the toxoid) None of the patients improved, 3 remained stationary and 8 became worse clinically and bacteriologically The authors have failed to confirm the beneficial results reported by some workers by treatment with diphtheria anti-toxin or toxoid

Faget and Johansen report on their extensive trial of the diphtheria toxoid in the treatment of leprosy in the National Leprosarium, Carville, Lousiana They had published a preliminary report in 1942, the present is a final report based on data collected over a long period

The method of administering the toxoid was that used by Collier The initial dose was 1 c.c, given subcutaneously This injection was repeated every two weeks, increasing each time by 0 5 c c until a dose of 3 c c was reached Thereafter the injections were continued at monthly intervals and the dose was reduced to 1 c c

The diphtheria anti-toxin titre of the serum of a number of patients was estimated before the treatment, and after a period of treatment It was found that leprosy patients as a group had a higher diphtheria anti-toxin titre than healthy adults It was also found that as a result of the injections of toxoid, there was a substantial rise in the

anti toxin level in the blood showing that the toxoid therapy was adequate as far as the production of anti toxin was concerned. How ever the results of treatment with toxoid indicate that the anti toxin produced by diphtheria toxoid in patients with leprosy does not neutralise the toxins of leprosy

This report is based on the treatment of three groups of patients The first group comprised of 12 patients subject to frequent lepra reaction. The second group included 70 patients half of these were given diphtheria toxoid and the other half (the control group) were given equal amounts of the broth from which diphtheria toxoid is made. All the patients of the second group however were under the impression that they were being treated with the toxoid The third group consisted of 183 patients all of whom were given the toxoid treatment.

In the first group the recurrent attacks of lepra reactions were unabated by the diphtheria toxoid injections The experience in this group of patients does not substantiate the claim that the toxoid treatment causes rapid subsidence of lepra reaction and prevents their recurrence.

In the second group the patients treated with the toxoid as well as those treated with broth were carefully examined before and after 10 months of treatment, and again later 5 months after the termination of one year of treatment. Amongst the toxoid treated patients 3 improved 8 were stationary and 24 worse. In the control group 3 improved 14 were stationary and 18 worse The toxoid treated patients did not show any advantage over the broth treated patients As a matter of fact in several ways they rather showed a disadvantage. No favourable influence of toxoid injection was noted on the occurrence or the severity of lepra reaction or on the relief of large neuritis

The 183 patients in the third group received toxoid treatment for 9 months. Only 6 of these patients showed any definite improvement 4 of these were of the tuberculoid type in which spontaneous improvement is common and the other 2 were already improving and were bacteriologically negative at the outset of this treatment 56 were classified as stationary with no material change in their condition 121 were definitely worse and have showed new lesions or evidence of an extension of an old lesion During the course of treatment of this group of patients the lepra reactions were frequent

The authors conclude their report as under —

From close observation of 35 patients treated with diphtheria toxoid for one year under carefully controlled conditions, and from the observation of 195 other patients treated with diphtheria toxoid from 6 to 15 months it is concluded that this treatment has no beneficial therapeutic action in leprosy

It is the unanimous opinion of the medical staff of the National Leprosarium that diphtheria toxoid is productive of no good, and is fraught with danger for the patients with leprosy

Carpenter Ackerman and Ashemburg report on the results of diphtheria toxoid treatment in experimental rat leprosy Their conclusion is that the subcutaneous injection of diphtheria toxoid failed to produce a beneficial effect on the course of experimental rat leprosy

Mills studied the thiamin excretion in the urine of persons living in Panama. He found that the thiamin excretion was below normal among people eating native foods. While persons recently arrived

from the United States had a daily thiamin excretion of 200–400 micrograms, permanent residents eating native Panama meats and other local foods are usually found to excrete less than 100 micrograms daily Excretion rates for the newly arrived Americans dropped from 200–400 micrograms down to 100 micrograms after about three weeks on the local foods

He further found that there was considerable thiamin unsaturation in the permanent residents of Panama eating the native foods Americans eating imported meats when given 3 milligrams a day of thiamin excreted almost half of this on the first day, while the residents of Panama on native diet took almost a week to reach that level of excretion

Suspecting a low thiamin content in the meat of the slow-growing tropical animals, Mills compared the effects of native and imported pork on excretion rates and found that greater thiamin excretion followed the eating of imported meat Samples of various animal products in Panama were then sent to an American laboratory for thiamin assay, and all values were found to be below normal

Considering all these facts Mills thinks it quite likely that a definite deficiency exists for certain B-vitamin fraction in the diets of tropical residents, and that this deficient intake is made even more serious by being coupled with a heightened requirement in the prevailing heat

The author concludes his article as under —

Moderate B-vitamin deficiency is probably widespread among tropical peoples thiamin excretion rates are at or below the lower limits of normal

Slow growing tropical meats are deficient as sources for thiamin, as compared to meats grown in cooler climates This coupled with a heightened requirement for certain of the B fractions in tropical heat poses a serious nutritional problem for tropical residents to consider

These various facts may have a bearing upon the handling of the leprosy problem.

Sir Leonard Rogers writes on the progress in the control of leprosy in the British Empire In 1934 the writer had recorded a brief history of the first decade of the work of B E L R A, of which he is one of the founders In the present article he has reviewed the leprosy situation in the various parts of the Empire The author points out that the review bears out the soundness and success of the general principles of employing voluntary measures where compulsion is not already in force, and of modifying compulsion in other areas to permit early non-infective cases to be treated as out-patients at hospitals and clinics

Muir writes on leprosy in the British West Indies and British Guiana Leprosy is believed to be introduced into this region by European invaders and by African slaves, and to a limited extent by indentured labour imported from India. Taking into consideration the morbidity and mortality alone leprosy cannot be considered as of major importance in this area In the whole area under review about 1,150 cases were isolated in institutions, 165 in Jamaica, 75 in Leeward Islands, 56 in Windward islands, 76 in Barbados, 400 in Trinidad and 375 in British Guiana The number of unisolated cases is difficult to judge accurately because of concealment and absence of any general systematic survey On a rough estimate there are probably less than 3,000 cases of leprosy in the whole area

The leprosy problem of individual colonies is discussed. There are institutions for leprosy in British Guiana, Trinidad Jamaica Barbados St Kitts Antigua Dominica St. Lucia Grenada and St Vincent Only in British Guiana and Trinidad are there whole-time medical officers in charge

The author summarises his articles as under —

1 Neither in the British West Indies nor in British Guiana can leprosy be considered from its morbidity or mortality to be a major disease But the mental distress which it causes both to the patient and to his relatives, makes it a disease which it is important to control and eradicate

2 The fact that in certain areas as for example in British Guiana and St Kitts, a consistent policy has brought leprosy to a position at least approaching control within a comparatively short period emphasises the importance of maintaining consistent efforts in other areas. The comparative smallness of the problem should give it precedence rather than cause it to be laid aside till other larger problems are solved

3 Leprosy is seen to be a disease associated with a low level of sanitation and standard of living it is aggravated by industrialism, especially when this involves living in congested dwellings migration from one place to another and especially visiting other countries where leprosy is common

4 The familial distribution of leprosy is favoured by its concealment a result of the attitude of the people toward the disease

5 For the control of leprosy the primary essential is better knowledge on the part of the medical profession In each unit (colony or island) where leprosy is still active there should be at least one physician who has made an intensive study of the disease Leprosy is no less difficult to understand than tuberculosis and an adequate knowledge is difficult or impossible to acquire without study at a suitable centre

6 The second essential step is the survey special attention being paid to the examination of school children and of contacts with open cases.

7 It is important also to make all institutions for segregation as attractive as possible by giving the best treatment and nursing available and by arranging for suitable and beneficial occupation

8 Facilities should be provided for suitable patients who so desire to be transferred to a central leprosarium which might serve all of the British West Indies and British Guiana

Doull *et al* report on the incidence of leprosy in the Municipalities of Cordova and Talisay in the Cebu province of the Philippine Islands. The prevalence of leprosy in these two municipalities has been reported on previously The authors explain the difference between prevalence and incidence The figures for prevalence are based on the results of a single physical examination of the inhabitants and indicate the magnitude of the current leprosy problem The figures for incidence on the other hand indicate the rates at which cases occur in specified periods of time.

The data for the study were collected in the homes and were supplemented by statements of patients in leprosaria and from records of these institutions All except a very few of the residents of these communities were examined in clinics established for the purpose The statistical methods employed are discussed in detail The life table method is used and the population is expressed in person years that is each year of life of each individual is regarded as a unit For a whole community the sum of the years of life recorded on the schedules constitutes the denominator only persons developing the disease while resident in the community are counted in the numerator The results are expressed as attack rates for 1 000 person years that is as the average number of cases per 1 000 persons observed for one year

The results of the study are summarised by the authors as under —

Incidence in the general population

1 The average annual incidence for all forms of leprosy for the period included on the schedules was 1 38 per 1 000 person-years for Cordova, and 1 11 for Talisay For both communities the average attack rate was equivalent to 1 20 cases per 1 000 persons annually

2 The peak of incidence occurred in the age group 10 to 14 years in both communities

3 For the cutaneous type for both communities the average annual incidence was 1 11 for males and 0 47 for females for the neural it was 0 39 for males and 0 34 for females

4 Excess prevalence of total leprosy in males noted in the previous reports, is demonstrated to be attributable chiefly to higher incidence in males than in females and not to longer duration of the disease in males In the cutaneous type however a minor part of excess prevalence in males is apparently attributable to longer duration of the disease

5 Cumulation of age-specific incidence rates to the age of 25 years yields an expected prevalence for all types of leprosy of 39 3 per 1 000 This is remarkably close to the prevalence rate (39 6) observed at the time of examination in persons of this age Beyond 30 years of age however, the higher mortality of leprosy patients than of other persons is indicated by the disagreement between actual and estimated prevalence rates

The risk of household exposure

1 For persons exposed in the household the average incidence rate for all types of leprosy was 5 35 per 1 000 person-years This is more than six times the rate for persons not known to have been subjected to household exposure

2 For age periods the highest incidence in both males and females occurred at 10 to 14 years both in household associates and in other persons The average age of onset however was lower for those exposed in the household than for other persons

3 When the primary case was cutaneous the risk of developing any type of leprosy for household associates was about eight times that for persons not exposed to leprosy in the household It was four times as great as when the primary case was neural

4 When the primary case was cutaneous the risk of developing cutaneous leprosy was about two and a half times the risk of contracting the neural form whereas when the primary case was neural the secondary attack rates for the two types were about equal

5 When the primary case was cutaneous the secondary attack rate for males for all types of leprosy was 7 99 per 1 000 person-years and for females 4 22 The secondary attack rate for cutaneous leprosy only was 6 16 for males and 2 38 for females No sex selectivity is indicated by the secondary attack rates for the neural type

6 The greatest disparity between the rates for the sexes appeared in the secondary attack rates for cutaneous leprosy in children of 5 to 9 years of age exposed to primary cases of the cutaneous type Here the rate for males was 9 77 and that for females was only 2 01 This suggests greater inherent susceptibility of males rather than difference in environment as the principal cause of sex variation

7 Cumulation of age specific attack rates to the age of 25 years for persons exposed to primary cases of the cutaneous type gives an expected prevalence of all types of leprosy of 293 per 1 000 for males and 140 per 1 000 for females Considering cutaneous secondary cases only, the expected prevalence for males is 235 per 1 000 and for females 83 These figures are very much higher than is generally appreciated and throw new light on the infectiousness of leprosy

Doull *et al* write on leprosy in Puerto Rico The date and manner of introduction of leprosy in Puerto Rico are unknown It is usually considered to have been imported from Africa in the early days of the slave traffic They conclude their article as under —

1 From the investigations so far made it is not possible to state the prevalence of leprosy in Puerto Rico with accuracy It is certain that more than one hundred cases exist and that for the most part these persons are in advanced stages of the disease From general knowledge of the disease it is fair to assume that there are at least as many unrecognised cases. If so the prevalence rate would be about 11 per 100 000 of the population This is a low rate in comparison for example with the Philippines where the estimated prevalence is about ten times as high

2 Even less can be said with assurance regarding the trend of the disease The recorded death rate indicates rather a static condition but such an index is unreliable The reported cases in recent years have averaged about eleven per year

3 The disease is widespread over the island with a predilection for the sea coast municipalities. Naguabo Patillas and Vega Baja have been focal centres and apparently this is still true San Juan and Ponce are centres of higher than average prevalence

4 Physical examination of 1873 school children in Naguabo Patillas Ponce and Vega Baja revealed no cases of leprosy It should be noted, however that a considerable proportion of children are not attending school and that those who were examined may not be representative of the child population of the respective municipalities. Among 105 family associates of known cases one neural case was found Two cases were discovered in Ponce and four in Naguabo among suspects sent for examination by physicians. Two of these were of the advanced cutaneous type and four were classified as neural

As a step towards more adequate knowledge of the prevalence of leprosy in Puerto Rico it is recommended that all the inhabitants of certain districts should be given a physical examination These districts should include certain barrios in Naguabo Patillas Vega Baja, Ponce and San Juan

There should also be initiated a current and thorough investigation of each case. Although prevalence may be much higher than we have indicated never theless the disease is *thin* in occurrence. Furthermore migration of the inhabitants of the island usually can be traced An exceptional opportunity is thus created to add materially to knowledge of the epidemiology of leprosy

Doull in an editorial discusses the interruption of leprosy work in many parts of the world due to conditions associated with the War This interruption is considered all the more serious since the number of persons engaged in the study of the disease has been small. In order to keep the work going as far as possible the American Leprosy Foundation has taken two important steps. The first step recognises Latin America as the most promising current source of scientific workers in leprosy fellowships are being offered to physicians of these countries for special study in leprosy in the United States. The second step is the decision to maintain a medium for the publication of original articles special issues of the *International Journal of Leprosy* will be published from time to time as sufficient number of manuscripts are received

REPORTS

A REPORT ON AN EPIDEMIOLOGICAL LEPROSY SURVEY IN BOMBAY PRESIDENCY

By DR I SANTRA

Introduction

For the last three years intensive leprosy surveys have been carried out in small selected areas in various parts of the country in order to obtain a more accurate idea of the incidence of leprosy, and the type distribution, age distribution, etc of the cases of leprosy The object of these investigations has been to study the clinical and epidemiological features of the disease in the different parts so that the leprosy problem in the various parts could be more accurately assessed. Such investigations have already been carried out in Assam, Punjab, United Provinces, Orissa, Central Provinces and Berar, Madras and Bihar The present work in Bombay is a part of this investigation Three months (Sept , Oct , Nov 1943) were spent in surveying an area with a population of about five thousand.

Selection of the Area

The rough sample surveys carried out by the Provincial Leprosy Officer in 8 districts of the Presidency during 1942 showed that the incidence of the disease varied from 1% to 5% and that the districts of Sholapur, East Khandesh and Satara have the highest incidence (5%) It was therefore decided to work in one of these districts, and the district of East Khandesh was selected for this purpose The village Hingona in Yawal Taluka of East Khandesh was selected for the survey as according to the report of the Provincial Leprosy Officer this village was heavily infected and its population was about 5,000 When the work was actually started it was found that the population of Hingona was only about 3½ thousand, and therefore a neighbouring village, Humberdy, was included in the survey to complete a population of 5 thousand Thus Hingona was selected on account of its being heavily infected, and Humberdy was only a chance selection The findings made in the two villages have been quite different

A General Description of Hingona and Humberdy

The village Hingona is situated on the Yawal-Faizpur Road, midway between the two It has a population of 3,580 distributed in 712 families The majority of the population (2,096) consists of Leva Patidars (Mahratta Hindus) The other chief castes are depressed classes 255, Muslims 432, Rajputs 170, artisan class 319 and others 308 The different castes live in different parts of the village

The diet of the people is very simple consisting mainly of jowar, chutney and butter-milk, and sometimes pulses The chutney consists of garlic and chillies Most of the people except the Rajputs and Moslems are vegetarians Fresh fish is unknown, but dry fish is available in limited quantities on bazar days

The economic condition of the people is fairly good The people seem to be industrious There is a fair number of cattle in the

village. Bazra jowar, maize pulses groundnut cotton and wheat are the chief products of the village.

Humberdy is a neighbouring village The people and their living conditions are similar to that of Hingona.

Previous Leprosy Surveys

A survey of village Hingona was made in 1937 17 cases were detected 10 neural and 7 lepromatous. The Collector has a list of 24 cases for Hingona and 2 for Humberdy this list is dated 9-2 42 The Mulki Patil of Hingona had 28 cases on his list of these 3 were found not to be cases of leprosy

The Present Survey and its Methods

It was originally proposed that the Special Leprosy Officer and the Red Cross Medical Officer would be available for help in this work but their services were not available as the former had resigned and the latter had joined the I A.M C The survey was therefore conducted with the help of two non medical assistants appointed locally One of the locally recruited assistants was a lady a passed dai The village Patel and Kamdars helped in the work.

Before the survey was commenced its purpose was explained to the villagers in a meeting Every day the people were visited in their homes before they left for the fields Their names were registered and the houses were marked in a map The men and children were examined by me the women were first examined by the lady assistant and anyone having a suspicious patch was later examined by me In the afternoon about an hour was devoted to the examination and treatment of other diseases. People absent in the morning were seen in the afternoon To examine all the people it was necessary to visit the houses several times.

The Findings made in Hingona

Gross findings —

Total population	Cases detected			Incidence %	Proportion of L cases.
	N	L	Total.		
3 580	41	10	51	1 42	19·7%

Clinical description of cases

Of the 41 neural cases 17 had flat patches (Ns) 13 (31%) had thick patches (Nt) and 11 had only sensory changes in the extremities and no patches (Na) None of these cases had severe mutilations and only one had a nerve abscess

Of the 10 lepromatous cases none had any eye or throat complication In 4 the extent of the disease was slight (L_1) in 2 moderate (L_2) and in 4 advanced (L_3)

Incidence of the disease according to age and sex

	Males		Females		Total.	
	Incidence %	Proportion L cases %	Incidence %	Proportion L cases %	Incidence %	Proportion L cases %
0–14	0 92	0 0	0 13	0 0	0 53	0 0
15–34	2 52	30 77	0 64	0 0	1 73	25 0
35 and over	2 0	27 77	2 03	18 75	2 47	22 22
TOTAL	1 69	25 58	1 14	15 0	1 42	19 6

Analysis of cases by type, sex and age

Age group	Males			Females.			Total for the age group			Total % of cases for the age group
	N	L	Total	N	L	Total	N	L	Total	
0–14	7	0	7	1	0	1	8	0	8	15 68
15–34	9	4	13	3	0	3	12	4	16	31 37
35 and over	8	3	11	13	3	16	21	6	27	52 94
TOTAL	24	7	31	17	3	20	41	10	51	99 99

Comments on the above analysis

Age and leprosy—Figures for both the incidence of the disease in the different age groups and the proportion of cases in the different age groups indicate that in this area the frequency of the disease rises with the increase in age It is less common in the age group 0–14, more common in the age group 15–34 and still more common in the age group 35 and over

Only about 16% of the total cases are found in children below the age of 15 while about 42% of the population belongs to this age group The incidence in adults therefore works out to nearly four times the incidence in children (2 1% in adults and 0 53% in children) The disease is not only less frequent in children than in adults but is also less serious, there is no lepromatous case in children and of the 8 neural cases in them 7 have the disease in a very mild form having only one or two patches each

The age group 15 to 34 contains 31% of the cases and the incidence of the disease in this group is 1 73% The age group above 35 contains about 53% of the total cases and the incidence of the disease in the age group is 2 47% The proportion of lepromatous cases is slightly higher in the 15 to 34 age group than in the age group above 35

Sex and leprosy—60% of cases were in males and 40% in females, the incidence of the disease in males being 1 69% and that in females

being 1 14% The disease in the males is also more serious than in females in males the proportion of lepromatous cases is 25 5% while in females it is only 15 0%

A rather unusual feature was the marked disparity in the incidence of the disease in the two sexes amongst children. There are 7 cases in 762 male children (19%) while there is only one case in 744 female children (13%) This is rather unusual because the incidence of the disease amongst boys and girls usually do not show such wide differences although there may be marked differences in the two sexes amongst adults

Leprosy in different castes

The incidence of leprosy in the different castes is shown in the following table —

Castes.	Population	No of cases.	Incidence %
Leva Patidars	2 096	38	1 81
Depressed class	255	2	0 78
Muslims	432	5	1 16
Rajputs	170	0	0·0
Artisan class	319	2	0·63
Others	308	4	1·29
TOTAL	3 580	51	1 42

Leva Patidars (Mahratta Hindus) constitute the majority of the population of the village and a majority of the cases of leprosy (38 out of 51) are found in them and they have the highest incidence (1 81%) There was no case of leprosy among the Rajputs numbering 170 The incidence in the other castes varies from 63% in the Artisan class to 1 16% in Moslems.

Local beliefs customs and traditions etc about leprosy

There are various gods worshipped by the people and their displeasure is believed to bring on the disease. The displeasure of the gods Maimazi and Bhabani is believed to cause leprosy If a person suspects that he has a patch of leprosy he shows it to a Bhakat (devotee of Bhabani or Maimazi) who gives his opinion. If he considers it to be a case of leprosy the person is advised to take a bath in the Tapti on a Tuesday or Friday and fast and worship for three days It is believed that some change in the patch will be noticed after 3 days if the condition is due to the god s anger and if no change is noticed in this period the disease is believed to be due to some other cause If the child of a person suffering from leprosy shows signs of the disease the disease is not attributed to the anger of the gods but to contact with a case of leprosy

There appears to be a custom of isolating cases of leprosy in the homes in a separate room or outside the village. If the person is not willing to be isolated the villagers often make his life miserable so that he may leave the village and go elsewhere. However for this purpose no distinction between neural and lepromatous cases is made.

Of the 51 cases detected in this survey, 7 persons have been living in isolation, 3 of them being infectious and 4 non-infectious Of the 7 isolated cases 3 are living at a distance of 6 miles in the Satpura Hills, and the other 4 are living with their families in the outskirts of the village Of the remaining 44 cases found living in the village itself, only 17 were known as cases before this survey was made Of these 17 known cases 10 cases (8 neural and 2 lepromatous) are reported to have been living in separate rooms in their homes

Findings at Humberdy

The main findings made at Humberdy are given in the following table —

Total population	Cases detected			Gross incidence
	N	L	Total.	
1 380	5	1	6	0 43

The figures for the area are too small for detailed analysis 5 of the cases were in males, and only one in female The one lepromatous case was amongst the males Of the 6 cases only one was a child below 15, and this is a neural case

Discussion

The incidence of 1 42% is not very high The proportion of lepromatous cases (about 20%) is fairly high A striking feature is the high proportion of the total number of cases (about 53%) in the age group of over 34, the incidence in this age group is 2 47%, compared with 53% in children, and 1 73% in the younger adults

These findings are very similar to the ones recently made in Kurud (C P) The following table gives the findings made in the two places —

Area	Pop Exd	Gross incidence %	Proportion of L cases %	Percentage of cases in the age group		
				0–14	15–34	35 and over
Kurud	5 498	1 16	20 0	14 0	23 5	62 5
Hingona	3 580	1 42	19 6	15 68	31 37	52 94

On the basis of the findings made in Kurud it was concluded that leprosy in Kurud was an old standing, not very serious, and possibly a diminishing problem The same remarks may be made about Hingona.

In Kurud, as in Hingona, the local people have been making attempts at isolation of cases of leprosy It is believed that this attempt, although not successful in controlling the spread of the disease, has had a limiting effect on its spread, and did not allow the leprosy problem to become more serious than what it is It is considered desirable that advantage should be taken of the existing customs

and practices of isolation in areas where they do exist, and that suitable methods of village isolation should be based on these customs.

Here in Hingona there exists public opinion in favour of isolation and isolation has actually been practised to some extent at least for the last 20 years. The people depending on their own initiative and resources, without any help from the local authorities have been doing what they could. Due to lack of knowledge however the right type of case has not always been isolated, and this has at times caused unnecessary inconvenience and hardship to some patients the isola tion has also not been effective in controlling the spread of the disease There is a very strong case for giving a proper lead and help to the people of the place for organising effective isolation

It is reported that sometimes back the local people and the District Officials had tried to start a centre for the isolation of the patients of the district and had approached the Government of Bombay for help in this matter They were however, told that since the present Leper Act was defective and needed modification and since the Government was considering a revision of this Act the Government would not be prepared to contribute anything towards the scheme before the Act was revised The Leper Act does need modification and revision but there is no justification for making this an excuse for postponing anti leprosy measure in any locality Com pulsion for isolation may have to be used in certain instances (and for this legal provisions should be made) but it is now generally re-cognised that the effective control of leprosy largely depends on voluntary measures.

Annual Report for 1943 of the District Anti-leprosy Committee, Bijapur

The report opens with the remark that in spite of many difficulties and handicaps incidental to the situation in the country arising from the present war and acute famine conditions prevalent in the district the Committee maintained a steady progress in its various activities during the year under report This was made possible by the grant of a maintenance allowance of Rs 2,500 from the Bombay Government, and a donation of Rs 3,000 from the Sir Dorabji Tata Trust, Bombay

The main activities of the Committee include the maintenance of a leprosy dispensary in the town, and a leper asylum with an attached outdoor treatmeut centre The asylum provides accommodation for 45 patients, and it remained full throughout the year The patients in the asylum are kept usefully employed in agricultural and industrial work In addition to giving useful employment to the patients these activities met a part of the cost of maintenance. There are 12 acres of land for tillage, a large flock of sheep, goats, poultry, etc, and a weaving department equipped with four handlooms During the year no expense was incurred on clothes, the institute was self-sufficient in this matter The total income from the sale of farm and industrial products was Rs 426, in addition clothes of the value of Rs 537 were supplied to the inmates, making a total income of Rs 964 from agricultural and industrial activities

The income during the year was Rs 7,922 including Rs 426 from the sale proceeds of agricultural and industrial products The expenditure during the year was Rs 4,286 including Rs 961 spent on improvements to the well

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Annual Report for 1943 of the Victoria Leprosy Hospital, Dichpali

The opening section of the report includes the following relevant remarks about the scope of activities of modern leprosy institutions —

'A modern leprosy institution is more than a hospital in the narrow sense of the term It includes educational recreational and occupational activities The departmental reports give details of these activities but we should just like to say here that we regard these of as much importance as the actual medical treatment for they improve the physique broaden the mind and change the outlook of the patients Some who come to Dichpali illiterate weak and depressed go out strong, mentally alert and more able to face the battle of life'

The report on medical activities state that 1,447 patients have been under treatment for various periods 170 patients have been discharged as symptom-free or disease arrested, 196 have been discharged on their own request after considerable improvement but before they could claim a medical certificate, 151 left without permission, 8 were dismissed for disciplinary reasons and 12 died. During the year there were 617 new admissions, and it is gratifying to note that 75% of these were infective cases The authorities would like to see a still further reduction in the admission of non-infective cases, but for various reasons they have to move more slowly in this matter

The report on agriculture education and recreational activities of the institution is abstracted below in full —

Agriculture

Agricultural work in a leprosy institution implies more than ordinary farm activities. It is a form of occupational therapy designed to improve the physique of the patients and to provide them with employment which is interesting In Dichpali the farm has always occupied a prominent place in the curriculum. Most of the patients find their sphere of communal service there and while engaged in agricultural pursuits an opportunity is presented to teach methods which are superior to the age-long methods of the villages. The Indian villager despite his lack of education is an intelligent man in regard to things which interest him, and many Dichpali ex patients have paid tribute to the value of the tuition on the hospital farm This last year has increased the importance of the work for the introduction of the communal kitchen with its demand for a liberal supply of vegetables and other farm produce has made necessary an intensification of the agricultural work. It is no easy task to make provision for eight hundred patients who must have an adequate liberal, well balanced diet all the year round but we are hopeful that by increasing the area under cultivation year by year it may be possible to become self-supporting

Crops —Rice continues to be the main crop and the yield during the past year has been fairly good 29 75 acres of land are under rice cultivation On the dry land jawar green gram and groundnuts were the principal crops and the returns of these were good though they might have been better had the rainfall been more evenly distri buted 20·78 acres of our land are devoted to these crops.

The garden land at present amounts to 3 25 acres but we hope to see this area greatly increased At present we grow brinjals ladies fingers carrots cabbages tomatoes beans *knol kohl* radishes, sweet potatoes chillies sweet limes papayas oranges limes and mangoes as well as a variety of leafy vegetables and while these may provide satisfactory variety the quantity will have to be considerably increased to meet our needs in the provision of a diet based on the standards of the Nutritional Research Institute at Coonoor

Fodder —It is no small task to provide enough fodder to meet the needs of the farm for there are 25 animals for which provision must be made. A considerable quantity of green grass is always available following the monsoon and this year some ground was brought under lucerne while a small area had guinea grass. There are about 240 acres of grazing land which is of great value.

Compost and manuring —More than 800 loads of compost were provided during the past year and this is of infinite value for manuring. Not only does the manufacture of compost provide useful work for the patients but it also offers a means of disposing of all sorts of rubbish from the kitchen and compound generally

Tillage —It has been said that it is harder to move earth than heaven but the patients during the course of the years have turned jungle land into a model farm. Land has been cleared of wild growth levelled laid off in plots ploughed and manured till Dichpali has been able to present an object lesson to those who have to stay while

under treatment and to the ryots from surrounding villages It stands as an example of what can be done by perseverance and hard work and we try to point out that our farm could be multiplied many-fold in Hyderabad State

Education

The treatment of leprosy is not a matter of injections only It is essential that where patients are segregated for a long period provision should be made for the development of mental and physical powers, else discontent and depression will retard recovery For the adult patients there are many useful and beneficial types of work but these are unsuited to children. For them education in the widest sense is all important To meet their needs there are classes in Telugu, Urdu, Marathi where they learn to read and write and count, demonstrations in the garden where the boys learn how to grow suitable vegetables, classes in sewing and mending where the girls can learn proficiency in these arts It is also imperative that there should be organised games and that entertainments should be provided

The primary school is conducted partly by trained teachers on the staff and partly by teachers who happen to be patients in the institution The boys and girls are keen to acquire education and many of them make amazing progress during their stay in hospital

For the children who are too young to attend the primary school there is a nursery school in a separate compound where there are toys, flower gardens, swings, etc.

Adults also are keen to learn and those who desire to attend school may do so in the afternoons and they have to be divided into literates and illiterates according to their background. The Laubach method is practised among the illiterate patients and it is very gratifying that so many learn to read in a short time

Recreation

Entertainments take the form of dramas enacted by the children, occasional lantern lectures and periodic cinema shows The boys and girls have various activities connected with the Girls' Life Brigade and the Boys' Brigade which are organisations of great value in furthering habits of cleanliness obedience and reverence The Brigades have periodic parades, camps, sports, meeting, etc , and the children love to be members of Brigade Companies

EPIDEMIOLOGICAL OBSERVATIONS ON LEPROSY IN C.P AND BERAR.*

By DR I SANTRA

Distribution of leprosy in villages

Two areas around Kurud (C.P) and Kashikhed (Berar) clinics were selected and all the villages situated within the area were surveyed. These areas probably do not represent the condition in the district for the simple reason that clinics are generally opened at places where a large number of cases are known to exist. The unequal distribution of leprosy in the different villages of the same area may give an idea of the general distribution of leprosy in the district and the variation found in the incidence of the two areas may give an idea as to how it may differ in C.P and Berar where the people are different from each other ethnologically climatologically and in their diet.

On looking at the spot maps one is at once struck how cases in villages around Kurud are localised to certain parts while in Kashikhed they are found spread over the whole village No village in both the areas is free from leprosy Out of six villages in Kurud all except one have lepromatous cases. In Kashikhed all the 9 villages surveyed have lepromatous cases but the proportion of lepromatous cases is very low The disease is distributed all over the village and it is difficult to understand how one case could have infected so many in all parts of the village

Type distribution in Kurud and Kashikhed

Localities.	No of cases.		Gross incidence %	Incidence of lepromatous cases %
	L	N		
Kurud Area—				
1 Kurud	4	25	1·08	0 15
2 Chamarla	4	11	1 85	1 49
3 Rakhi	2	4	1 26	0 42
4 Charra	1	1	0·23	0·11
5 Umarda	2	7	2 31	0 58
6 Karharpuri	0	3	0·84	0·00
Kashikhed Area—				
1 Kashikhed	3	22	5·29	0 63
2 Kamnapur-Ghusli	1	27	4·60	0·16
3 Asegaon	4	49	7 57	0·57
4 Wadhona	1	16	2 02	0·12
5 Shalanapur	1	8	5 69	0·63
6. Nalgondi	1	10	2·93	0·27
7 Saula	1	23	3 18	0 13
8 Arvi	3	40	6 48	0·45
9 Bhilli	4	22	8·60	1 31

* A report on epidemiological leprosy surveys in the Central Provinces by Dr Santra was published in our last issue (January 1944) The present report is a continuation of the previous one and in it Dr Santra discusses some of the findings reported previously —*Ed*

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4 Charra	1	1	0·23	0·11
5 Umarda	2	7	2 31	0 58
6 Karharpuri	0	3	0·84	0·00
Kashikhed Area—				
1 Kashikhed	3	22	5·29	0·63
2 Kamnapur-Ghusli	1	27	4·60	0 16
3 Asegaon	4	49	7 57	0·57
4 Wadhona	1	16	2·02	0·12
5 Shalanapur	1	8	5·69	0·63
6 Nalgondi	1	10	2·93	0·27
7 Saula	1	23	3 18	0·13
8 Arvi	3	40	6·48	0·45
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From the above figures it will be seen that gross incidence in the Kurud villages is low, varying from 0 23% to 2 31% In Kashikhed area it is high, varying from 2 02% to 8 60%, but the incidence of lepromatous cases is not so markedly different in the two areas This may mean that while in one area the lepromatous cases are more communicative in the other area they are less so This point will be discussed later

That the spread of the disease may depend upon the amount of mixing of the healthy persons with known cases, is noticed from the fact that at Asegaon where the incidence is 7 57% there is a section of the village having 36 houses where there is no leprosy The affected part of the village has 53 cases spread all over The section free from leprosy is situated on the other side of the road about 350 steps away from the main village It consists of 36 families of Mohammedans, Hindus and their low caste servants A generation back these people came from U P and knowing that there were many lepers in the main village tried to avoid contact with the villagers as far as possible

Leprosy amongst different castes

The incidence is definitely more among the lower castes than in the upper castes In Kurud the number of upper class people was small and there was no case among them In Kashikhed prevalence of leprosy among the upper and middle class is about the same In both the areas the incidence is highest amongst the low castes Below are the figures —

	Upper Class		Middle Class		Lower Class	
	Popul	Inci	Popul	Inci	Popul.	Inci.
		%		%		%
Kurud	320	0 00	3,760	1 01	1 299	1 9-
Kashikhed	1 600	4 31	1 726	4 16	1 477	6 22

Leprosy in families

The word family has been here used to include all the people who mess together If several people related to one another live under the same roof but have three separate kitchens they are considered to be three families In the Chattisgarh, young men after marriage separate from their parents They may live in the same house but cook separately In such cases they have been counted as separate families On an average a family consists of about 4 members. The largest number of cases in a family in Kurud is 3 and in Kashikhed 4. In some cases the disease runs in families, and in many families several numbers are affected

History of leprosy in some villages

Kashikhed—Sixty years ago the village consisted of 7 families, there being no lepers among them The villagers grew castor-oil

plant in plenty extracted oil just enough for their use and sold the seeds. This attracted the Teli caste from other parts Gradually about 25 families of Telis came from the districts of Chanda Buldana. There were about 40 oil presses in the villages Railway communi cation oil mills growth of cotton plantation have destroyed this village industry but this immigration infected the village since the source of leprosy in the village is traced to three lepers two among the oilmen and another in a Gawari family who had a lepromatous case and came from Yeotmal district.

Bhili —An old woman of 65 years (a case) says that when she came as a bride to this village there was only one case. This man died six years back at the age of sixty The villagers do not remember of any other case previous to him At present there are 26 cases in the village.

Kamnapur-Ghusli —Twelve years back Madhu Gond a lepromat ous case came from another village and settled down as a labourer here. He was the first case amongst Gonds and all the present cases among Gonds say that they got it by mixing with him

Amongst the Mahars certain cases are traced to Devaji Mahar (L case) who died 15 years back

Shaulama —Pandu Thakre a lepromatous case died 25 years back. Panduvar Chandrabhan another influential man like him died about 16 years back Both were moving around the village with impunity

Cases among the Mahars are traced to Madhu Mahar a leproma tous case who died eight years back There are several cases amongst his relatives.

Contact and leprosy

It is usual to group the history of contact into intra familial and extra familial In this report a slightly different procedure has been adopted. Contact with parents brothers and sisters uncles and aunts and close relatives has been considered as familial With others it has been noted as village contact. By contact is meant contact with a lepromatous case If a boy has leprosy and his father mother or some relatives were neural cases and if there is no history of association with any other lepromatous case he is recorded as not giving any history of contact. The figures are given below —

	Total No of cases.	% of cases where history of contact was obtained				% of cases who gave no history of contact
		Familial.	Village	Casual.	Total.	
Kurud	64	54%	14%	2%	70%	30%
Kashi khed	236	29%	12%	0%	41%	39%

The number of people in Kashikhed affected through family members is decidedly small. In Kurud intrafamilial contact appears to be an important factor

House infection

An investigation has been made as to what percentage of the adults and children living in the same house with a lepromatous case has developed the disease The results are shown in the following table —

	No of people who lived with a lepromatous case		No who developed the disease and their %	
	Adult	Child	Adult	Child
Kurud	20	12	4 or 20%	3 or 25%
Kashikhed	51	33	16 or 31%	7 or 21%

The average number of people living in a house where a lepromatous case lives is higher in Kashikhed, viz , 4 4 than in Kurud, viz 2 46

Husbands and wives as sources of infection

At Kurud 4 and at Kashikhed 3 wives stated that they got the disease from their husbands No other history of contact could be obtained in these cases No man reported to have got the disease from his wife It is usual for a wife to be driven away if she gets leprosy, the reverse may take place rarely

Unusual sources of infection

In one case a daughter-in-law gave history of infection from her father-in-law, and son-in-law from his mother-in-law These are rather unusual sources as by custom the parties are not supposed to come in close contact. Considering cases like this and the number of cases (59%) in Kashikhed who could not give any history of contact, it appears that in susceptible persons even casual contact may give rise to the disease The question whether leprosy is an air-borne infection or not may have also to be considered

Neural cases as sources of infection?

Many cases gave history of contact with neural cases Neural parents had neural children It may not be fruitless to enquire whether neural cases during the stage of reaction can transmit the disease

Leprosy in women and children

In both areas leprosy amongst women and children had a low incidence and mild type Not a single case of leontiasis was found amongst them

Clinical consideration

Kurud —Out of 64 cases, 57 cases started as neural and 7 started as lepromatous Six neural cases subsequently became lepromatous A case that starts as lepromatous generally starts with multiple non-[illegible]thetic patches, in some of the cases the first symptom to be noted

was oedema of fingers and toes and face Two lepromatous cases had affections of the eyes

Of the 51 neural cases 25 had patches (18 simple and 7 minor tuberculoid) 18 had no patches but only anaesthetic areas (Na) and 3 had both patches and anaesthetic areas.

Kashikhed—Of the 236 cases 19 were lepromatous and 217 neural Of the neural cases 161 had patches (128 simple and 33 tuberculoid) 31 had anaesthetic areas (Na) and 20 had both patches and anaesthetic areas A majority of the cases had the disease in a mild form and the popularity of the treatment in the area is considered to have played a part in this. This impression receives support from the finding made in a group of 20 cases 8 miles away from the clinic and not getting any treatment on the whole the disease in these cases was more severe than in the above cases getting treatment.

Preventive method practised by the villagers.

The Kashikhed clinic was the result of an agitation by the people that the disease had grown recently

Land has been acquired by the Kashikhed Village Uplift Committee for the purpose of isolating infectious cases. Three cottages were under construction when the survey was being conducted.

Of the 19 cases in the area one was living in a shed built in his own compound But in general neither the villagers nor the cases themselves were keen on isolation.

At Kurud conditions were different It appears that some sort of isolation measures is in existence there from olden times. Probably because of this the poor who have no separate house to live and find it difficult to live in the village leave for cities to beg This fact may have been responsible for the concentration of the missionary leper asylums in Chattisgarh (5 of the total of 7 in C.P) and the general impression created thereby that in C.P Chattisgarh had the highest incidence of the disease although the census figures for 1931 and subsequent surveys have shown a higher incidence in Berar than in Chattisgarh

Out of 13 lepromatous cases in Kurud living condition of 7 is given below (1) B T female 25 unmarried highly infectious case lives isolated in a small hut near her father's house works in the field and earns her wages. (2) B S male, married wife lived with him but soon after our examination when the wife knew that it was a danger to live with her husband left him (3) L. male, formerly highly infectious rendered slightly infectious by treatment wife left long ago lives apart in a separate room has a son aged 15 who has no signs of the disease (4) B K male 28 moderately infectious not able to marry (5) B J male 45 highly infectious case lives alone no children wife left (6) B H male, highly infectious lives alone no children wife was taken away by another man (7) S.P male 53 a Malguzar highly infectious has a large family but on the commencement of the disease sent away all except his wife to another village. These members numbering 20 have been examined and found free from leprosy

From the above it would appear that there already exists a custom of isolation of cases of leprosy and what we have to do is to make use of this custom and to build on it our leprosy control work

CORRESPONDENCE

To

THE EDITOR,
'LEPROSY IN INDIA'

DEAR SIR,

I have gone through the letter of Dr R G Cochrane, dated 6th Sept, 1943, published in your issue of January, 1944. Questions raised by Dr Cochrane have been replied by the editor These discussions have brought to light many interesting points There are however two points in Dr Cochrane's letter which I could not follow —

(1) He has written 'If the skin is a necessary medium for the development of progressive leprosy (meaning lepromatous leprosy), may it not be a *sine qua non* that well-nourished skin is a better pabulum for the multiplication of the bacilli than an under-nourished one' In another paragraph he has written 'Lepromatous leprosy seems to occur in the well-nourished as frequently as it does in the under-nourished' These two statements appear to be contradictory If the well-nourished skin is a better pabulum for the multiplication of the bacilli it is only reasonable to expect lepromatous cases in the well-nourished and neural cases in the under-nourished Or at least lepromatous cases should occur in the well-nourished more frequently than (and 'not as frequently as') in the under-nourished If that be so then diet becomes the deciding factor in the course of the disease, i e better diet and better nourishment will favour the development of lepromatous leprosy, and bad diet and malnutrition will have an opposite effect But this does not fit in with actual findings because lepromatous cases are often found in the ill-nourished, and neural cases are more frequently seen in the well-nourished

(2) He has written Leprosy in the lepromatous form can be described as a parasitic invasion of the reticulo-endothelial system and it appears to me that for progressive leprosy to develop the bacilli must constantly pass from internal foci in the body to the skin'

While Dr Cochrane has advised others to avoid 'smoke screens' in leprosy, quite unconsciously he has put forward a hypothesis which is no better than a smoke screen Has he anything to support this theory? What are the foci in the body from where the bacilli constantly pass to reach the skin and what is the evidence?

If the skin is a better pabulum for the multiplication of leprosy bacilli it is only likely that they multiply in the skin and from there gradually pass on to other parts of the body In that case there is no need to formulate that bacilli come out of some internal foci about which we know nothing It is true that in lepromatous cases bacilli are often found in the internal organs but at that stage they are also

found in the skin nerves lymphatic glands etc. and all of them may serve as foci for dissemination of bacilli to other non affected parts.

Yours sincerely
D N BOSE
Medical Officer
Asansol Leper Hospital and Settlement

To
THE EDITOR
'LEPROSY IN INDIA
CALCUTTA

DEAR SIR

In war time when the usual antiseptics recommended for the treatment of ulcers of leprosy have become very costly or even unavailable the following substitutes may be used with good results

(1) *Lepromatous ulcers* —These are caused by breaking down of nodules or lesions in the skin or mucous membrane. Special care should be taken to treat these as they discharge enormous numbers of bacilli.

(*a*) Ulcers of the skin —The ulcers are cleaned with potassium permanganate lotion (1 in 1 000) and then either gauze soaked with 15% of tannic acid solution is applied or the ulcers are painted daily with 5% silver nitrate solution and bandaged. When the oozing of the serum ceases the ulcers are painted with 2% solution of mercurochrome, bandage being omitted

(*b*) Ulcers of the mucous membrane particularly of the nose— Nasal douche is given twice a day with a solution of sodium bicarbonate (1 dr to a pint) followed by instillation into each nostril of the following preparation— Camphor Gr 20 Menthol Gr 20 Oleum Hydnocarpus (crude) 1 Oz.

(2) *Trophic ulcers* —

(*a*) Superficial ulcers —These are due to bursting of blisters or bullae caused by the destruction of nerve fibres or injury burns scalds on the anaesthetic areas. These are cleaned with potassium permanganate solution (1 in 1 000) dressed with normal saline and bandaged If necessary injection of hydnocarpus oil may be given around the ulcers and along the damaged nerve The very superficial ulcers are dealt with 10% boric ointment.

(*b*) Deep ulcers.—If the superficial ulcers are neglected they are contaminated with secondary organisms causing cellulitis increase in size of the ulcer producing sloughs giving offensive smell and burrowing the deeper tissues causing ultimately necrosis of the underlying bone. These are

cleaned with the same lotion as stated above and dressed twice a day with E C or with a mixture of E C and saturated solution of magnesium sulphate The necrosed bone, if any, is removed Sulphonamides are given when needed A warm bath or compress may have to be applied in some cases Injection of the oil is given as mentioned above Giving rest to the affected region is considered an essential factor in treating the trophic ulcers

J BANSWAR, L M P,
Medical Officer, Bhagalpur Leper Home

ERADICATION OF LEPROSY

To

THE EDITOR,
'LEPROSY IN INDIA',
CALCUTTA

On a modest estimate leprosy patients in India number one million of whom about 2½ lakhs are in an infectious condition, but the combined accommodation in all the leprosy institutions is for only about twelve thousand patients As the State may not be able to provide for the isolation and treatment of the very large number of infectious patients who are a constant source of danger to others, it has been suggested by some that self-supporting agricultural colonies should be established where such patients may live separately and may do some work to contribute to their maintenance Though the idea appears to be good its application is not easy There already exist some colonies for leprosy patients in certain parts of the country In these, and in many of the ordinary homes for the care of the leprosy patients, agricultural and industrial work is done by the patients The work provides the inmates with helpful and congenial occupation, and at the same time meets a small part of the cost of their maintenance But the colonies and homes have never been self-supporting

Patients physically handicapped and incapacitated for hard work, are unable to produce sufficient for their upkeep The homes in which they are accommodated are generally situated in proverty-stricken areas and get little or no local help For instance, in the 'Mission Agricultural Leper Colony', Saldoha, Bihar, the patients are of a tribal origin, free from caste restrictions regarding occupations to be pursued and able to turn their hands to many jobs, under Mission supervision the patients build their own homes in small hamlets, cultivate the land, keep cattle, etc and manage their own affairs, nevertheless the colony is nothing like self-supporting

Even more difficult than the maintenance is their segregation Many patients have wives or husbands and children dependent on them and are unwilling to leave them. This leads to the spread of the disease to contacts and birth of children who are later infected.

In circumstances such as those mentioned above if 'Leper colonies' are to be formed, those organising them will have to seek more help

from the Government as also from the public contributions from the people being particularly needed as owing to the war large organisations like the Mission to Lepers are threatened with a decrease in the funds they have hitherto obtained from America England, and other countries. The organisers should enlist the support of influential and sympathetic members of the general public to persuade patients to live separately Where this is not possible measures have to be taken to prevent children being born to leprosy patients In some parts of the world colonisation by leprosy patients has been encouraged and male patients have been allowed to marry only after sterilisation Sometimes such patients have been allowed or encouraged to adopt leprous children No attempt at work along these lines has yet been made in India Leprosy Councils in different parts of India should investigate how far control by sterilisation is practicable.

K. N RAO,
Missionary Medical College Hospital Vellore

Leprosy in India

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EDITORIAL NOTES

An Apology

We owe an apology to our readers for the delay in the publication of this the July issue of *Leprosy in India* and for the reduced size of the issue. Under the Paper Control (Economy) Order of 1944 the size of the journal has to be considerably reduced from July 1944 the number of pages per issue to be only 30% of the average number of pages during the preceding 12 months. This means that we can publish only 12 pages for each issue every 3 months. This reduction in size will be a great handicap

Since this is the only journal dealing with the important problem of leprosy and anti-leprosy work in India, a representation has been made to the authorities concerned for getting exemption from the restrictions imposed on the size of this journal under the Paper Control Order It is hoped that, in view of the very useful purpose served by the journal it will be possible to obtain exemption, at least to some extent.

It was originally intended to postpone the publication of the July issue till the matter was finally decided This has already caused a considerable delay and it is now felt that waiting for the final decision may cause much further delay We are therefore bringing out the July issue according to the restrictions of the Control Order This has necessitated the omission from this issue of a number of contribu tions previously accepted for the July issue. Let us hope that it will be possible to obtain some exemption from the restrictions and that the future issues of *Leprosy in India* will be much bigger than the present one.

Sulphonamides in the Treatment of Leprosy

Sulphonamides are being extensively used in the treatment of various diseases caused by pathogenic micro-organisms. They have been tried in the treatment of leprosy also However till recently no encouraging results have been reported of the use of these drugs in the treatment of leprosy

Faget and Johansan (1942)* reported on a trial of sulphonamide derivatives in the treatment of leprosy in the National Leprosarium, Carville. They found the drug to be very toxic and to have no curative effect on leprous lesions. These drugs however proved effective in the treatment of secondary infections com plicating leprosy and of secondarily infected leprous ulcers. Other workers, including some workers in India have arrived at similar conclusions.

Recently Faget *et al* (1943) † have reported favourably on the results of treat ment of leprosy with promin, a sulphonamide derivative In the experience of these authors promin has proved to be the best of all the sulphonamide derivatives, including sulphanilamide sulphathiazole, sulphapyridine, and sulphadiazine, which

* Faget, G H. and Johansan P A. *Pub Health Rep* 1942 57 1892
† Faget *et al* *Pub Health Rep* 1943 58 1729

been used in the National Leprosarium, Carville. They regard the treatment promin as the most encouraging experimental treatment ever undertaken at ational Leprosarium

n our present issue, we are reprinting this article of Faget et al For want ce we have excluded the detailed case histories included in the original article. ne benefit of our readers, however, we have summarised these case histories

pe	Duration of the disease in years	Condition at the commencement of promin therapy	Duration of promin treatment in mons.	Results
natous	12	Little previous improvement during 9 years of hospitalisation.	26	Gradual disappearance of discreet nodules on face The patient now appears to be entirely free from leprous lesions Skin smears became negative after 24 months of treatment but a few acid fast bacilli were found in one subsequent smear
natous	12	No recent advance in the disease	26	Facial nodules definitely decreased in prominence and size Nasal obstruction due to leprous rhinitis almost completely cleared up Improvement in general health
	13	A far advanced case showing a progressive aggravation of the disease during the previous 13 years	24	Chronic ulcers of legs and other parts completely healed Nasal obstruction due to leprous rhinitis completely relieved No definite improvement in leprous lesions Improvement in general health
	9	A far advanced case getting worse	24	Chronic ulcers healed up Nasal obstruction and bleeding relieved. Laryngeal condition improved. Improvement in general health
matous	15	Moderately advanced, showing no evidence of improvement	19	Nodules on arms and legs, smaller and flatter A few nodules disappeared
l	6	Moderately advanced, without any definite improvement	18	Manifestations of leprosy gradually lessened Smears became negative after one year's treatment One smear showed some bacilli subsequently but after that smears were negative
l	13	Moderately advanced the disease had recently become worse	19	A slight decrease in the size and elevation of the nodules Improvement in general health.
	17	Moderately advanced condition stationary	17	Healing of leprous ulcers Leprous infiltration of face diminished.

Type	Duration of the disease in years.	Condition at the commencement of promin therapy	Duration of promin treatment in mons.	Results.
Mixed	7	Disease moderately advanced and taking an unfavourable course	17	Ulcers healed partly Skin infiltration subsided
Lepromatous	19	Disease moderately advanced stationary for a year	16	Numerous nodules became flattened or disppeared entirely
Lepromatous	10	Moderately advanced the disease progressing unfavourably	16	Subsidence of lepromatous plaques of the face and a decrease in infiltration of the legs.
Mixed	10	A far advanced case the disease getting progressively worse each year The principal reason for starting promin treatment was the seriousness of eye complications leprous keratitis and iridocyclitis which were destroying his sight.	16	Keratitis and iridocyclitis improved with definite improvement in sight. Nasal discharge and epistaxis due to leprous rhinitis ceased
Lepromatous	17	Moderately advanced case the disease progressing unfavourably	15	Only slight improvement. Slight subsidence of infiltrated lesions.
Lepromatous	12	Moderately advanced case showing no tendency to improvement. The patient has a diffuse infiltration of the whole body	14	Only slight subsidence of the diffuse infiltration
Mixed	18	The disease far advanced with total blindness. Threatened respiratory obstruction from advancing leprous laryngitis was the reason for starting promin therapy	13	Laryngeal and nasal conditions improved Leprous ulcers healed. Smears bacteriologically negative for the last 3 months.
Lepromatous	8	Moderately advanced.	13	No demonstrable improvement.
Mixed	15	The disease far advanced.	13	Leprous iridocyclitis subsided, but no improvement in leprous keratitis. The condition of the patient worse than at the beginning of treatment.
Mixed	18	The disease far advanced. Rapidly failing vision due to keratitis and iridocyclitis was the reason for trying promin.	13	Iridocyclitis subsided but no improvement in keratitis Nasal obstruction due to rhinitis greatly relieved. Ulcers of leg healed
Mixed	10	Moderately advanced case the disease becoming steadily worse Leprous laryngitis was the reason for instituting promin treatment.	12	Laryngitis improved Ulcers healed. Nodules became smaller

Type	Duration of the disease in years.	Condition at the commencement of promin therapy	Duration of promin treatment in mons	Results
Lepromatous	8	Disease moderately advanced, condition stationary	12	Subsidence of infiltration and nodules of ear lobules First negative skin test after 11 months' treatment.
Mixed	12	Moderately advanced the disease progressing unfavourably	12	A decrease in the amount of infiltration and nodulation of the face and body Suffered from several acute lepra reactions
Neuromacular	4	Moderately advanced	12	Macules faded to some extent Nasal obstruction markedly relieved Smears less strongly positive

From the above table it will be seen that all the cases, treated with promin, were advanced, bacteriologically positive cases of long standing, in most of whom the disease was getting progressively worse. Several of the cases were suffering from chronic leprous ulceration, leprous keratitis, leprous iridocylitis, leprous rhinitis with ulceration, nasal obstruction and epistaxis The results obtained in these cases indicate that promin is very effective in the treatment of chronic leprous ulceration and leprous conditions of eye, nose and throat, which are possibly caused by secondary infections However, promin does not appear to have a marked effect on the actual leprous infiltration and nodulation.

The authors of the paper have concluded that while no direct evidence has been obtained of a specific bacteriostatic or bactericidal action of promin against the leprosy bacillus the drug appears to inhibit the progress of leprosy in a considerable percentage of cases They consider it as an advance in the right direction in the treatment of the disease. However, before the therapeutic value of promin in leprosy can be properly assessed, it is very essential to have further and more extensive studies on the matter

Even if promin is found effective in leprosy, its toxicity appears to be a definite drawback to its routine use in the treatment of leprosy, especially when it is to be given over a prolonged period. Promin is more toxic when given by mouth than when given intravenously The authors had therefore to abandon the oral route in favour of the intravenous route. The intravenous administration, however, is also not free from toxic reactions, the most important of which is the slow destruction of the red blood cells Three-fourths of the cases, treated by the authors suffered from marked anaemia, necessitating treatment with iron and liver, with or without cessation of promin therapy Obviously it will be necessary to search for a derivative of promin which should be much less toxic than promin itself

Instruction course in Leprosy

The next annual course on leprosy arranged at the School of Tropical Medicine, under the auspices of the Indian Council of the British Empire Leprosy Association, will be held from 6th to 18th of November, 1944, provided number of candidates are forthcoming Applications for admission to the should be sent to the Officer-in-charge, Leprosy Research Department, ool of Tropical Medicine, Calcutta, to reach him by the end of September, 1944.

REPRINTED ARTICLE

THE PROMIN TREATMENT OF LEPROSY

By G H FAGET *Senior Surgeon* R. C POGGE *Asst Surgeon (R)* F A JOHANSEN *Surgeon (R)* J F DINAN *Passed Asst Surgeon (R)*, B M PREJEAN *Passed Assistant Dental Surgeon (R) and* C. G ECCLES *Passed Assistant Surgeon (R) United States Marine Hospital (National Leprosarium) Carville La.*

(*Pub Health Rep* 1943 58 1729)

Promin, the sodium salt of p p diaminodiphenylsulfone n.n. didextrose sulfonate, has been used in experimental tuberculosis in guinea pigs with remarkable success. Its clinical trial in human tuberculosis as a chemotherapeutic agent has met with at least promising results Its experimental use in the treatment of leprosy was commenced by the writers over 2 years ago and at present it is felt that promin is a therapeutic agent worthy of further trial in human leprosy The writers have had no experience with the drug in murine leprosy but in this type of the disease the reports are suggestive of slight action.

In our experience promin is the best of all the sulfonamide derivatives, including sulfanilamide, sulfathiazole, sulfapyridine, and sulfadiazine, which have been used in the treatment of leprosy at the National Leprosarium. It can be regarded as the most encouraging experimental treatment ever undertaken at the National Leprosarium. The writers are not in a position at this time to state that it possesses any specific action upon Hansen s bacillus. They consider it an advance in the right direction in the chemotherapy of leprosy and hope that further synthesis of the sulfa chemicals will produce a product which has specific properties against M. leprae and M. tuberculosis.

Our experimental study was made possible through the co-operation of Parke Davis & Co the manufacturers of promin which was supplied gratis for this experiment through Dr E. A. Sharp the Director of the Department of Clinical Investigation of this firm.

TECHNIQUE.

Promin can be given orally or intravenously By oral administration it is more toxic, and much larger doses are tolerated by the intravenous route. In our preliminary studies promin was given by mouth to a group of 10 patients. Small doses of ½ to 1 gm. were tolerated for such short periods that therapeutic effects seemed unlikely by this method of administration. Severe reactions particularly hemolysis were so easily provoked that this mode of medication was soon abandoned. Since then the intravenous injection has been favored in all cases. The great majority of patients under treatment have received from 1 to 5 gm. daily for 6 days a week Sunday excepted. Most of the patients were given the 5 gm. dose and the course of treatment was continuous for months with only short intervals of rest of 1 to 2 weeks three times a year In the case reports in calculating the average daily dose these rest periods and Sundays are included.

Studies of the promin concentration in the blood showed a rapid decline. It was found that only traces remained 6 to 8 hours following the intravenous administration of 5 gm. of promin.

TOXIC MANIFESTATIONS.

The intravenous administration of promin is not free from toxic reactions. The most important of these is a slow destruction of the erythrocytes. This effect is generally delayed for several weeks but one must be constantly on the alert for its development. It is our practice to do complete blood counts routinely every 2 weeks on every patient on this treatment.

In the writers' experience, anemia occurs in 46% of cases after 6 weeks of intravenous promin therapy The longer the continuous course of treatment, the greater the number of anemic patients It was observed that during the complete course of treatment the erythrocytes fell to 3 5 million or less in 71% of cases and in 9% they fell below 3 million. In the great majority of these cases antianemic therapy, with or without cessations of promin, was successful in raising the red blood cells and hemoglobin to their former levels

Satisfactory maintenance of blood levels can be attained in several ways A fall of the red blood cells below 4 million is an indication to start the patients on inorganic iron, ferrous sulfate, or ferrous carbonate, in adequate doses This usually restores the red blood cell count and hemoglobin level, as occurred in 66% of our cases If the erythrocytes continue to decrease, an oral liver and iron preparation is substituted for the iron This proved adequate in readjusting the erythrocytes and hemoglobin in 60% of cases not responding to iron alone A certain percentage of patients do not respond to these simple measures In such instances and whenever the red blood cells decline below 3 million, promin is discontinued temporarily and liver extract is administered parenterally in addition to iron orally This treatment is continued until the erythrocytes rise above 3 5 million, when it is considered safe to resume promin therapy at the rate of 2 gm a day, provided the liver and iron are continued

According to Higgins promin in guinea-pigs exerts a direct toxic effect on the erythrocytes, leading to their destruction and removal from the blood by the spleen. He found that promin did not permanently damage the bone marrow and regeneration of erythrocytes proceeded during continuous administration of the drug

The writers have observed that in some cases the institution of promin therapy actually resulted in an increase in the red blood cell count and the hemoglobin percentage. It is believed that in such cases the healing of secondary infections results in a general improvement in the patient's health, one of the manifestations of which is the lessening of secondary anemia

Besides a decrease in the red blood cells, leucopenia has been encountered. It occurred in 3% of the cases under treatment Severe agranulocytosis did not develop, but it was thought best to discontinue promin promptly whenever the white blood cells fell below 3,000 In one case promin treatment was abandoned because the response to injections of pentnucleotide and liver extract was unsatisfactory

A routine bimonthly urinalysis is another precautionary measure instituted in this experimental study, since other sulfonamides are known to cause renal impairment So far, no evidence of kidney irritation or damage has been demonstrated by the routine urinalyses, which are supplemented by occasional renal function tests whenever deemed indicated Toomey and Tokacs were not successful in attempts to produce urinary concretion in monkeys by intravenous injections of promin doses six times as large as those recommended for human beings

After hemolysis, the most important toxic reaction was the development of an allergic dermatitis This generally manifested itself as a diffuse maculopapular eruption which was accompanied by intense itching Dermatitis medicamentosa is, of course, a cause for temporarily discontinuing promin therapy In the majority of these allergic patients, desensitization is feasible After the eruption has completely disappeared, promin is resumed in minute doses, 0 1 gm , intravenously By gradually increasing the dose over a period of approximately one month, it is possible to arrive at therapeutic doses of 2 gm daily without further allergic reactions. In some cases full doses of 5 gm are eventually reached without a of dermatitis

rgic dermatitis occurred in 16% of the patients under study Two- of these have been desensitised at present In only 3% of cases the e proved entirely unsuccessful, the others are in the process of desensitisation. Another manifestation is allergic rhinitis, which developed in one patient After months the sneezing episodes following each injection of promin ceased

Other untoward reactions headaches and nausea are generally mild and ephemeral. Nausea occurred in 35% of cases. It is transitory in nature and can be prevented by injecting the drug more slowly Vomiting followed nausea in only 7% of cases It also responds to slower injection, up to 1 minute being required to administer 5 gm. of promin intravenously Several patients complained of headaches, which were never severe.

An increase in erythema of leprous plaques was noted in 3% of the cases This accompanied the first few weeks of treatment and gradually subsided. Its cause is unknown. Acute leprae reactions with fever and the appearance of erythema nodosum occurs less frequently with promin than with most previous experimental treatments or than with the routine chaulmoogra oil injections. It was the cause of discontinuing promin therapy in only four cases

An exacerbation of an iridocyclitis occurred in 10% of cases. In all of them the patient had experienced frequent previous attacks or iridocyclitis. This drug seems temporarily to increase the severity of the ocular inflammation, which is generally followed by improvement. In only one patient the exacerbation of iridocyclitis initiated by promin persisted longer than 1 month

A generalised lympyadenitis was another unusual toxic manifestation which occurred in one patient. Reduction of the dose of promin to 1 gm. resulted in the subsidence of the glandular enlargement.

Clinical Material.

No attempt was made to select minimal or moderately advanced cases with favorable prognosis. Thus only a few cases of neural and maculoanaesthetic types are included in the study All patients treated were bacterioscopically positive at onset and many had never had a negative bacteriologic report during the entire previous period of hospitalization. Many patients volunteering for treatment had far advanced lepromatous and mixed types of leprosy with poor prognosis. The disease in the majority of cases was showing a definite trend toward aggravation before the institution of promin therapy Several cases were selected because of certain complications which it was thought might be favorably influenced by the promin. Among these important complications were Leprous keratitis and iridocyclitis, with pending loss of vision in some cases leprous rhinitis with ulcerations repeated epistaxis and partial obstruction of nares leprous laryngitis with threatening suffocation chronic leprous ulcerations and lepromatous lesions and ulcers of the tongue, palate, gums and lips which usually respond poorly to other forms of treatment. The effects of promin in these complications of leprosy have, for the most part been good.

Patients with eye nose and throat complications were examined before and during the course of treatment in the eye, ear nose and throat clinic, and those with oral lesions were examined in like manner in the dental clinic.

The eye, ear nose, and throat specialist (J.F D) reports that many patients under promin therapy showed a marked improvement in nasal breathing The initial examination in these patients reveals ulcerations of the nasal mucous membrane and excessive mucous secretion, which on drying and crusting produces blockage of the nasal passages. There is also a tendency to frequent epistaxis. After a course of promin it is observed that the ulcerations, which are probably due to secondary infection, heal the excessive secretion and crust formation subside, and nasal bleeding ceases.

Another observation is that promin seems to benefit eye complications of leprosy It is noted that patients on promin therapy do not have so many attacks of acute iridocyclitis as formerly Two patients have shown by slit lamp examination that leprous punctate keratitis has disappeared to a considerable extent.

Objective improvement in vision has been marked in only one patient. This patient started with only light perception and projection in one eye, the other totally blind Shortly after the institution of promin parenterally the

iridocyclitis and edema of the cornea gradually improved. This continued until on the last examination it was found that he had recovered 20/100 vision in his good eye.

Many patients with advanced lepromatous and mixed leprosy show evidence of leprous laryngitis The symptoms are huskiness of voice, vocal weakness, dryness of the throat with unproductive cough, and finally attacks of respiratory difficulty Six patients with advanced leprous laryngitis were started on promin intravenously, and all of them improved, especially in the quality of their voices and the restoration of comfortable respiration. It is felt that two of these patients escaped a proposed emergency tracheotomy because of the beneficial relief attributable to promin therapy

In the dental clinic it was noted that in several patients leprous lesions of lips, tongue, gums, and hard and soft palate have diminished and in four patients completely disappeared after prolonged treatment with promin Some mucosal ulcerations of the hard and soft palate and of the lips have healed under the influence of promin.

The following table is a summation of the results of intravenous promin therapy in the patients whose case histories are reported here, * each of whom has taken at least 12 months of treatment

TABLE I

Type	Number	Improved	Stationary	Worse	Bacteriologic reversion from positive to negative
Mixed far advanced	6	3	2	1	1
Mixed moderately advanced	5	4	1		1
Lepromatous, far advanced	1	1			
Lepromatous, moderately advanced	9	6	3		3
Neural, moderately advanced	1	1			
TOTAL	22	15	6	1	5

Not included in these case reports or in table 1 are 46 additional patients who have taken a shorter course of promin intravenously Some of them are beginning

TABLE 2

Type	Number	Objective improvement	Stationary	Worse	Bacterioscopy negative	Treatment discontinued.
Mixed far advanced	4	1	3			2
Mixed moderately advanced	14	6	6	2	1	6
Lepromatous far advanced	5	3	2		1	
Lepromatous moderately advanced	13	8	4	1	2	2
Lepromatous minimal	4	3	1		1	1
Neural, moderately advanced	5	4	1		2	
" minimal	1	1				
TOTAL	46	26	17	3	7	11

* For want of space the case histories have been excluded from this article.

to show signs of improvement, and a few have reverted from a positive to a negative bacterioscopy The duration of treatment in this more recent group of patients varies from 2 to 11 months and averages 8 months. The preliminary results of intravenous promin therapy in this group are briefly indicated in table 2 Also shown in this table are the number of patients in whom bacteriologic tests became negative and those in whom treatment was discontinued for one reason or another

In these more recently treated cases it can be seen that an attempt was made to select a more favourable and less advanced type of disease

There were 16 patients altogether in whom treatment was discontinued for various reasons. This number includes a few patients taking less than 2 months treatment who are not otherwise included in this report. The reasons for discontinuing treatment were as follows Refusal of patient to co-operate, 5 repeated acute leprae reactions with erythema nodosum 4 patients absconding (improved nodular cases) 2 exfoliative dermatitis 1 leucopenia 1 previous advanced nephritis 1 and increased icteric index in a patient with previous hepatitis due to sulfanilamide, 1

The following table gives pertinent data on all cases which reverted from a positive to a negative bacterioscopy under the influence of promin therapy

TABLE 3

Registration Number	Months of treatment before first negative report.	Amount of promin required before first negative report in grams.	Number of negatives.	Registration number	Months of treatment before first negative report.	Amount of promin required before first negative report in grams.	Number of negatives.
869	24	1 926	1	1 417	8	365	1
1,229	13	298	1	1 500	8	427	1
1 413	24	*519	2	817	7	794	1
575	9	948	3	1 123	6	692	3
1 196	11	756	1	1,492	6	240	3
1 343	10	485	1	1 514	6	373	1

* In addition to 233 gm. of sulfathiazole.

Because leprosy is a chronic disease subject to periods of spontaneous remissions more or less prolonged, it may be difficult to determine whether improvement under any new experimental treatment is entirely due to the remedy under study or not. However the writers feel that the large number of patients showing improvement in contrast to the small number in whom unfavourable progress was made under promin therapy cannot well be explained on the basis of spontaneous improvement alone.

To test this impression a control experiment was undertaken with a prominlike drug, Internal Antiseptic 307 which was administered orally in capsules to one group of patients while a placebo lactose with a trace of quinine, in similar capsules was given to another group of patients. The placebo was similar in appearance and taste to the active drug, and none of the patients taking it suspected that they were not being actively treated. Internal Antiseptic 307 chemically is sodium 4, 4 -diaminodiphenyl-sulfone-2-acetylsulfonamide. Being closely related chemically to promin, it was found to have a similar action in leprosy It was chosen for oral administration instead of promin which is too toxic when given by mouth. Internal Antiseptic 307 is a Parke Davis product and was furnished gratis by this firm for this experiment.

There was less objection in this institution to the administration of a placebo orally than by the intravenous route, as it would have been more difficult to manage a control series of patients on intravenous injections without arousing their suspicion

The group of patients taking the I A 307 and those of the control group were closely matched as to type and stage of the disease The dosage of the drug and of the placebo were the same, varying from 5 to 15 gr daily and averaging 10 gr It was necessary to use these small doses of I A 307 to obviate toxic reactions, since this drug has cumulative properties The patients of both groups were handled in exactly the same manner During the course of treatment complete blood counts and urinalyses were done every 2 weeks on all patients of both groups Antianemic therapy was administered to patients of either group whenever indicated by the laboratory findings

After a period of over 8 months it became apparent that there was a difference in the condition of the two groups of patients While the course of the disease continued unabated in the control group, it was checked in a considerable percentage of the treated patients Complications of the disease, such as ulcerations, rhinitis, laryngitis, and iridocyclitis, frequently improved under I A. 307 but were unaffected in the control patients A comparison of the results after more than 9 months of treatment is given for the two groups in table 4 In this table under complications are included chronic ulcerations, leprous rhinitis, leprous laryngitis, and iridocyclitis

TABLE 4

	Internal Antiseptic 307	Control
Number of patients	20	20
Improvement in leprosy	6 (30%)	1 (1%)
No change in leprosy	5 (25%)	9 (45%)
Leprosy worse	3 (15%)	5 (25%)
Improvement limited to complications	5 (25%)	
Complications worse	1 (10%)	5 (25%)
Bacterioscopy becoming negative	2	

Data in the above table seem to indicate that improvements in leprosy under promin and prominlike drugs cannot be attributed only to spontaneous remissions in the course of the disease

CONCLUSIONS

Promin is the sulfonamide drug which thus far seems to possess to the greatest extent some chemotherapeutic properties against leprosy

While no direct evidence of a specific bacteriostatic or bactericidal action against M leprae has been demonstrated, it has been observed that promin appears capable of inhibiting the progress of leprosy in a considerable percentage of cases As yet no case of leprosy has become arrested under its influence

It is found that promin can be safely administered intravenously for prolonged periods, provided the blood and urine are examined frequently When these precautions are taken, toxic manifestations are relatively rare and mild The most important of them, hemolysis, if recognised early, is usually controllable and not a cause for discontinuance of the treatment.

Further experimental and clinical studies on the treatment of leprosy with promin must be conducted before more definite conclusions can be drawn as to its therapeutic value

It is not claimed that promin is a specific for leprosy, but in the writers' estimation is an advance in the right direction in the therapy of this disease.

Promin can be considered to have opened a new avenue in the chemotherapy of bacterial diseases It is hoped further synthesis of sulfa compounds will produce a substance which will succeed in saving countless lives in this still fruitful field of medicine

REPORTS

THE ANNUAL REPORT FOR 1943 OF THE INDIAN COUNCIL OF B E.L.R.A.

The Annual Report for 1943 of the Indian Council of B E.L R A. is divided into four parts Part I contains the Report of the Governing Body, Part II the Report of the activities directly under the Indian Council, Part III, the Headquarters Accounts and Part IV the Report of the Provincial Branches. Below we reproduce the Report of the Governing Body presented by its Chairman Lt.-Col. E Cotter, C.I.E I.M.S

General

Although war conditions have produced difficulties in the way of developing the anti-leprosy campaign of the Association, yet speaking generally the quality and quantity of the work have been maintained at a satisfactory level. Due to conditions in the Pacific, the *International Journal of Leprosy* published in the Phi lippines had to suspend publication. This has led to lack of touch with the outside workers and to difficulties in the production of *Leprosy in India* An important section of *Leprosy in India* is that on Current Literature and material for this section was provided mostly by the *International Journal of Leprosy* and the *Leprosy Review* the *International Journal of Leprosy* has ceased publication, and the *Leprosy Review* is also not received regularly The foreign circulation of *Leprosy in India* has also been affected, and due to this and to the necessity of economy in the use of paper the number of copies printed has been reduced from 700 to 550 The war conditions have affected the work in another way also The annual leprosy course under the auspices of the Association, usually held towards the end of the year at the School of Tropical Medicine Calcutta had to be postponed this year because a sufficient number of doctors did not apply for admission to the course, and no nominations were made by the Provincial Branches of the Association. However a special course was held at the School of Tropical Medicine from 17th to 29th May for doctors deputed by the Bengal Branch 13 doctors attended the course and 10 passed the examination held at the end of the course.

The activities of the British Empire Leprosy Relief Association are of two kinds (*a*) the work directly under the Indian Council at the School of Tropical Medicine, Calcutta and elsewhere, and (*b*) the activities of the Provincial Branches. Originally certain activities, such as research, training of doctors and organisation of propaganda etc. were undertaken only by the central organisation. A noticeable development during recent years has been that some of the Provincial Branches specially the Madras Provincial Branch have been taking a prominent share in these activities. The Central activities and the activities of the Provincial Branches are reported separately later on in this report.

During 1943 Dr John Lowe relinquished his appointment as a Research Worker under the Association. Dr Lowe joined the Association as a Research Worker in 1933 and became the Head of the Leprosy Department of the School of Tropical Medicine in 1935 on the retirement of Dr Muir The Governing Body takes the opportunity of placing on record their appreciation of the valuable work done by Dr Lowe during a period of ten years. Dr Dharmendra an officer of the Medical Research Department of the Government of India has taken his place.

At the request of the Government of Orissa Dr Dharmendra and Dr Santra paid a short visit to Orissa to help the Government in formulating their future anti leprosy programme for the province. In 1938 the Orissa Government sanctioned an anti leprosy scheme at a cost of about Rs 30 000 per annum, in the first instance for five years. At the end of this period it was considered desirable that before taking any further steps the work of the past five years should be carefully examined. The working of the existing anti leprosy scheme was reviewed, and suggestions for its improvement were made. The services of the central organisation

Epidemiological studies—(*a*) Epidemiological studies of the Bankura Investigation Centre have been continued. The findings made during the last six years have been analysed. In this area, as in other similar areas, statements have frequently been made that leprosy is rapidly increasing The study has shown that in spite of the absence of any effective isolation measures, there is no evidence that leprosy is increasing in the area

Interesting and important observations regarding the clinical course of the disease have been made, and are summarised later The study has brought out the great prognostic value of the lepromin test in cases of leprosy, during the period under study the type of the disease has changed from the neural to the lepromatous in eight cases, and all these eight cases had been lepromin negative when tested before the change.

It appears that sufficient epidemiological data about the disease in the area has been collected at the centre, and that the centre may now enter the second phase of its activity, i.e to attempt to control the spread of the disease in the locality by introducing suitable methods of isolation. If it could be demonstrated that by isolating most of the infective cases in the area under investigation the incidence of the disease could be considerably lowered in due course, it would be a great advance and would greatly stimulate anti-leprosy work in the country

(*b*) Dr Santra, the Propaganda Officer of the Association, has continued accurate leprosy surveys of the whole population of selected small areas This year he has worked in two areas in Bihar, and in one area in Bombay His findings have shown that the marked disparity of the incidence of the disease in the two sexes which is often reported is not a constant feature in all areas In the two areas in Bihar the proportion of the cases in the two sexes was about equal, in the area surveyed in Bombay 63% of the cases were found in males.

Publication and Propaganda—The propaganda material published by the Association is stocked at and issued from the Red Cross Depot through the courtesy of the Indian Red Cross Society In addition to the free issues, articles of the value of Rs 1,749-6-3 were sold during the year as against Rs 592 in the previous year This material comprised 13,914 books and leaflets, 768 posters and 480 slides 2,500 copies each of the two propaganda leaflets, 'Five Questions about Leprosy' and 'Fight Leprosy with Knowledge', in Urdu were published for general distribution. A new book entitled 'Popular Lecture on Leprosy' is under print and will be released shortly

The quarterly journal, *Leprosy in India*, continues to serve a useful purpose This journal is produced in the Leprosy Department of the School of Tropical Medicine, and is issued from headquarters. It is a quarterly record of the study of leprosy and of anti-leprosy work in India and in other countries On account of the non-receipt of foreign literature on leprosy, specially the *International Journal of Leprosy*, the production of *Leprosy in India* has become more difficult because of paucity of suitable material However, the high standard of the publication has been maintained On account of the restricted foreign circulation and of the necessity of paper economy, the number of copies printed has been reduced from 700 to 550 Its publication cost the Association Rs 852 during the year, of which a sum of Rs 512 was recovered from subscriptions and advertisements The *Leprosy Review* which is published by the British Empire Leprosy Relief Association, London, is also circulated in India

The Provincial activities

The reports of the Provincial Branches are abstracted in Part IV of this report. These reports indicate that a steady progress is being made in the various provinces activities, such as treatment of cases of leprosy, propaganda, teaching institutions, surveys, etc, have been continued The epidemiological, and immunological studies in Madras have continued, the details of these will be found in the Report of the Madras Provincial Branch. An outstanding

development during the year in Madras has been the establishment of Special Leprosy Departments in the teaching hospitals, the Leprosy Department at the General Hospital Madras is fully organised and the organisation of the Leprosy Departments at the Stanley Medical College Hospital Royapuram Madras and at the King George s Hospital, Vizagapatam are proceeding

Finance

The audited statements of accounts together with the Honorary Treasurer s explanatory remarks will be found in Part III of this report. These accounts show that the financial position of the Association continues to be satisfactory As in previous years more than half the income was distributed to Provincial Branches for expenditure on local activities whilst the amount retained at headquarters was spent on objects which benefit the country as a whole

Governing Body

Lt.-Col. E Cotter C.I E I.M.S Public Health Commissioner with the Govern ment of India continued as Chairman of the Governing Body and Mr K. Sanjiva Rao C.I.E. and Sardar Bahadur Balwant Singh Puri O B.E as Honorary Treasurer and Honorary Secretary respectively There have been five vacancies on the Governing Body during the year which have been filled as follows —

1 Lieut.-General G Wilson Director of Medical Services in India *vice* Major-General A. C. Munro retired.
2 Major-General J B Hance Director-General Indian Medical Service *vice* Lieut -General Sir Gordon Jolly resigned.
3 Dr Dharmendra Officer in Charge of the Leprosy Department School of Tropical Medicine Calcutta *vice* Sir Muhammad Zafrullah Khan resigned.
4. Lieut.-Colonel H. Williamson Surgeon to the Viceroy, *vice* Lieut.-Colonel Elliot transferred
5 Lieut.-Colonel C. A. Bozman Additional Public Health Commissioner *vice* Major C. K. Lakshmanan transferred

Leprosy in India

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EDITORIAL NOTES

Sodium Morrhuate and E C C O in the treatment of Leprosy

The two drugs at present in common use for the special treatment of leprosy are the hydnocarpus oil (plain or creosoted) and ethyl esters of hydnocarpus oil (iodised or creosoted) In countries where the oil is not produced sodium salts of fatty acids of the oils are sometimes used as they are easier to export because of their small bulk. Intramuscular and subcutaneous injections of these salts are painful and hence they are usually given by the intravenous route However intravenous injection of these salts is apt to cause endophlebitis and obliteration of veins.

During the early days of the treatment of leprosy by injections various other preparations had been tried, but were ultimately given up Most of these drugs have gone out of use but occasionally one comes across references to the use of some of these drugs even at the present day not only by individual medical men but also by some leprosy clinics and hospitals. Two such preparations which need a special mention in this connection are Sodium Morrhuate and E.C C.O

Sodium morrhuate is the sodium salt of fatty acids of cod liver oil. It was introduced in the treatment of leprosy by Rogers in 1919 in the belief that the power of destroying the acid fast bacilli possessed by the unsaturated fatty acids of hydnocarpus oil was shared by other unsaturated fatty acids. He found that unlike the sodium salt of fatty acids of hydnocarpus oil, sodium morrhuate was quite non-irritant when given intravenously but that it was equally effective in the treatment of leprosy Sodium morrhuate may be of some value but experience with this preparation has shown that in the treatment of leprosy it is inferior to hydnocarpus preparations Because of this it has never been popularly adopted and extensively used in the treatment of leprosy No reference to the use of sodium morrhuate in the treatment of leprosy is found in the modern literature on leprosy For the special treatment of leprosy hydnocarpus preparations have been the mainstay for centuries. In this connection the International Congress on Leprosy held in Cairo in 1938 observed that Hydnocarpus oil and its esters administered intramuscularly subcutaneously and intradermally remain so far as our present knowledge goes the most efficacious drug for the special treatment of leprosy[1]

The other drug that deserves mention here is E.C.C.O which is a mixture of hyl esters of hydnocarpus oil camphor creosote and olive oil. 1 to 2 c.c. of the ethyl esters are diluted with 3 c.c. of olive oil and 0·5 gram camphor and 0 5 c.c. of double distilled creosote are added as anodyne and antiseptic. The addition of a diluent was necessitated by the fact that undiluted esters were found too painful for continued use This dilution with an inert oil was made on the analogy of dilution of the hydnocarpus oil itself The method of parenteral injections of hydnocarpus oil was introduced as early as 1894 by Tourtoulis Bey an Egyptian worker but its general adoption was greatly delayed by the fact that the oil available then and for some years subsequently was found too painful for injections In an attempt to

overcome this difficulty the hydnocarpus oil was combined with other inert oils and anodyne substances The best known of these mixtures is that of Heiser and Mercado The Heiser-Mercado mixture consisted of hydnocarpus oil, camphor and resorcin Later, it was found that the irritant properties of the oil were caused by the presence in the oil of the decomposition products, and that the oil expressed from fresh ripe seeds was quite suitable for injection without any diluent Consequently undiluted hydnocarpus oil (plain or creosoted) has totally replaced the oil mixtures

Similarly the esters when first introduced were found too painful for injections and like the oil were diluted with inert substances and anodynes This was how Muir introduced the E C C O mixture containing ethyl esters, olive oil, camphor and creosote Later with the improvement in the methods of preparing the esters it was found that dilution with inert substances was no longer necessary This led to the replacement of the E C C O mixtures by creosoted esters In the Philippine Islands and some other places the iodised esters have been very extensively used with satisfactory results

Thus the use of both sodium morrhuate and E C C O in the treatment of leprosy originated in the Leprosy Department of the Calcutta School of Tropical Medicine With further experience, however, this department has now for long given up the use of these two preparations However, not a few private medical men and some leprosy clinics still seem to prefer these preparations to the undiluted oil or esters

There appears to be no justification for a drug like sodium morrhuate to have any place in the routine treatment of leprosy since we know that so far, the hydnocarpus preparations are the most efficacious drugs for the special treatment of leprosy For the use of E C C O also there appears to be no justification because dose for dose the mixture contains much less of the active therapeutic agent For example, a patient getting 5 c c of E C C O receives only 1 5 c c of the ethyl esters, while another patient getting 5 c c of the ethyl esters derives benefit of the full 5 c c.

ORIGINAL ARTICLES

A SIMPLE METHOD FOR THE PREPARATION OF IODISED HYDNOCARPUS OIL

By DR. A SHAMA RAO, *Leprosy Officer, Hyderabad State, Hyderabad-Deccan*

While hydnocarpus oils and their derivatives are extensively used as special drugs for the treatment of leprosy opinion is as yet divided as to the relative merits of the various preparations We find, therefore, different preparations finding favour in different parts of the world Pure chaulmoogra group of oils are extensively used in Japan In the Philippines the iodised esters have found favour, while in India creosoted hydnocarpus oil is the standard antileprotic drug

If properly refined according to the method of Perkins (1927) the oil of commerce loses all its irritating properties and the resulting product does not require the addition of any analgesic substance before injection As in Japan pure oil could be injected in large weekly doses Ethyl esters have an inherent irritating effect which is corrected by the addition of iodine The question whether iodine enhances the effect of ethyl esters has been reopened by Lara and Samson (1934) They consider that iodine not only acts as a corrective but that it has a real therapeutic value

Owing to the abnormal prices of creosote and its unavailability, workers in India trying other substitutes Dharmendra and Santra (1944) have recently reported trial of iodised hydnocarpus oil. Preparation of iodised ethyl esters require ch care If the temperature and time of heating are not properly controlled

(Cole 1933) sunlight and exposure to air make the iodised esters more irritating The method of preparation of iodised hydnocarpus oil given by Dharmendra and Santra is a modification of Cole's method for esters (1929) A small quantity of sterilised oil is mixed with a known quantity of iodine powdered in a mortar and ground into a fine paste The paste together with the requisite quantity of oil is then transferred to a stoppered flask and kept at a constant temperature of 140°C for 30 minutes On cooling the brown product is filtered tested for free iodine and sterilised in ampoules It would be seen that such a method is quite unsuitable to a travelling officer with little equipment and less of assistance Some years back when I was in charge of the Karwan Leprosy Clinic I devised a very simple method for iodising hydnocarpus oil The iodised oil prepared by this method was extensively tried for a period of two years in the Karwan Clinic which is a whole-time clinic working 6 days a week with a daily attendance of 60 to 80 patients The preparation was found quite satisfactory and I am publishing this method of iodisation in the hope that it may be of help to other workers like myself who are handicapped by want of facilities.

The method of iodising the oil is as follows 40 grs. of chemically pure iodine is added to 1 oz 2 drs of pure ether in a 2 oz stoppered bottle and shaken well for about a minute The iodine dissolves immediately The iodised ether is then added to 1 lb of sterilised and cooled pure hydnocarpus oil (supplied by the Ernakulam Trading Co) On shaking the resulting iodised oil is of a brown colour and can be utilised immediately for injection On exposure to air and sunlight the oil loses its transparency and assumes a dirty green colour after the lapse of two weeks Neither the brown nor the green oil shows the presence of free iodine when tested in the usual way with chloroform and starch solution * and even after the lapse of a few months no precipitate is observed in any of the above samples. Though my usual procedure was to iodise oil every other day I have extensively tried the samples which have turned green and find no difference in their therapeutic value

The oil iodised according to the above method has been injected intradermally as well as subcutaneously twice a week in the usual doses. The slight induration and hyperpigmentation caused by intradermal injections disappear in about two weeks The freshly prepared sample is easier to inject than the pure oil and no case of ulceration or lepra reaction has ever been noticed by me

During the past four years the oil iodised as above has been used in a very large number of cases of leprosy of all types viz. lepromatous simple neural and tuberculoid. While early cases of all types respond favourably to iodised oil advanced cases especially of the lepromatous type give highly variable results This remark however applies not only to iodised oils or esters but to almost any drug used in the treatment of leprosy

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1 Cole H I (1929) *Philippine Journ. Sci* 40 p 503
2 Cole H. I (1933) *Internat Journ Leprosy* 1 p 159
3. Dharmendra and Santra, I (1944) *Leprosy in India* 16 p 54
4 Lara C. B and Samson J G (1934) *Internat Journ Leprosy* 2 p 81

We have tested for the presence of free iodine several specimens of oil freshly iodised by the above method and have always found free iodine with chloroform and starch solution However if after the addition of the iodine the oil is sterilised in an autoclave it turns dark green and no free iodine is found. Intradermal injections of the oil iodised according to the above method, both before and after sterilisation, were found to be a little more painful than similar injections of oil iodised by the method wherein a temperature of 140 C. is used for ensuring a proper chemical combination of iodine and oil. Since for the raising of the temperature to 140°C. the only apparatus needed is a thermometer and a sand bath it is considered that this method should be preferred if possible —*Editor Leprosy in India*

THE PROBLEM OF LEPROSY IN THE TEHRI GARHWAL STATE, U P

By I SANTRA (*Leprosy Research Department, School of Tropical Medicine, Calcutta*)

INTRODUCTION

For a long time it is known that leprosy is very prevalent in the State Leper asylums situated in British India, adjacent to the State, had always drawn a large proportion of their inmates from Tehri Garhwal Even after the Punjab Government decided not to admit any cases from outside the province, the leper asylums at Tarn Taran, Sabathu and Ambala have today 24, 71 and 31 cases from this State Dehra Dun has 12 such cases Thus at present at least 138 cases of leprosy belonging to the State are found in the leper asylums in British India

The people of the State, because of its isolated geographical position and uninterrupted Hindu dynasty for the last 1,400 years, have been able to retain more of their original culture than what has been possible in most other parts of India, from time immemorial people have been observing some kind of segregation, such as asking the advanced cases of leprosy to leave the village and live on its outskirts

A real attempt by the State to control the disease began in 1916 A census of lepers was made in that year, and 473 cases were recorded On 26th May, 1916, the Regency Council passed a resolution on the prevention and treatment of leprosy, and a leper asylum was opened at Barahat in Uttar Kashi The custom of isolating cases of leprosy in the outskirts of villages was to be practised more rigorously, the relatives of the patients were tied by a bond to observe the restrictions, and if they failed the leper was to be taken by force to Barahat colony and maintained there-at the cost of the relatives On the 31st January, 1917, the President of the Council paid a flying visit to Barahat, he found only 19 inmates although it was believed to have 117 He remarked that the phenomenal decrease was due to the fact that the monthly charge of Rs 5 from the relatives of the patient for his maintenance was not paid and he was taken away home

In 1919 the matter was again taken up and on 19-2-19 the following resolution was passed unanimously by the Regency Council 'The Council approves of the segregation of lepers being made compulsory in Patti Mugarsanti as an experiment The lepers will be segregated in the leper asylum at Barahat, for each leper so segregated the leper's village will be required to contribute on the following scale Grain 12 chattacks a day, Dal 2 chattacks a day, and Ghee or oil one seer a month If the contribution in kind is not paid the equivalent sum will be levied in cash The contribution is to be paid in a lump sum when the harvest is ripe' A Sub-Assistant Surgeon was to visit the villages of the Mugarsantipatti, submit the names of all lepers to the chief Court for issuing orders of detention at Barahat colony, copies of which were to be sent to the Malguzars, Patawaris, C M O and the Superintendent of Barahat Leper Colony It is not known if the scheme was ever enforced, but at present there does not exist any colony at Barahat

Sometimes before 1930 the lepers themselves formed another colony at Munikirti within a mile of Rishikesh (Dehra Dun) The Durbar on the 8th August, 1930, made a provision for a grant of Rs 4 per month to those lepers of the State who would stay at Munikirti, but those who liked to live outside the villages (supported by relatives) were allowed to do so It is not known for how long this grant was paid, at present no such grant is being made since the condition for the grant was that the patients should not go about for begging, and this condition is not being fulfilled by the patients

THE PRESENT INVESTIGATION

In 1943 the State authorities wanted to organise the anti-leprosy work in the State, and they got in touch with the British Leprosy Relief Association for this purpose As a result, a study was planned by the Research Worker of the British Empire Leprosy Relief Association and the Public Health Minister, but due to

various reasons it could not be carried out in full. The details of the work done are given below

General

Ten days were spent at the Munikirti colony Five weeks were spent in surveying 40 villages situated in 8 pattis lying mostly in the western part of the State the part reported to have more leprosy than other places. Only the villages which were known to have cases and were within 3 miles from the main road were selected for the survey There were many villages adjacent to the surveyed villages which were reported to have no cases and therefore not visited The surveyed villages were thus deliberately selected and therefore the findings made in these villages are not applicable to the State as a whole. The villages surveyed have a total population of 7,082 and an incidence of 2 05% of leprosy Detailed figures are given later

The Munikirti Leper Colony

At Munikirti all the inmates were examined, and enquiries were made regarding their economic and social conditions and their past histories. Seven vaids and 1 compounder of the State were present during the investigation at the colony These 8 men were instructed in the diagnosis and treatment of leprosy

Number of inmates and their domicile—One hundred and sixty seven persons live in Munikirti, of these 157 are cases of leprosy 9 healthy children of leper parents and 1 healthy wife of a patient Six of the cases could not be examined as they had gone on a begging tour

Out of the 151 cases examined 117 belonged to this State (79 males and 38 females) 30 belonged to British Garhwal 3 to Almorah and 1 to Nepal. The reason given by the British Garhwal patients for coming to Munikirti was that here they got more food and enjoyed freer life than at the leper asylum at Srinagar in British Garhwal.

The type-distribution of the cases—Of the 117 patients belonging to the State 53 (45%) were infectious and 64 non infectious.

The living conditions and maintenance—The houses have been built by the patients themselves and most of them are low thatched and clumsily built. The patients receive free ration from the Punjab Khetra and Kali Kambli Khetra the two religious organisations which look after the comforts of the pilgrims to Rishikesh. The monthly ration consists of atta 9½ seers rice 4 seers salt ½ seer spices ⅛ seer molasses ¼ seer and ghee ¼ seer They have to beg to obtain money for purchasing dal, vegetables and clothes For this purpose they sit on the road-side from Munikirti to Lakhmanjhula and surround every car or tonga that happens to stop at Munikirti. Generally they do not go to Rishikesh except on the days they have to get their fortnightly ration from the Khetra and then also only to the place where the food is distributed

The medical care of the patients—There are no arrangements for giving treatment to the patients Some of the inmates during their previous stay in leper asylums had received training in giving injections and dressing ulcers With a little expenditure arrangements for treatment could have easily been made with the help of these persons.

The social life at the colony—Most of these persons had developed leprosy in adult life and had to quit their villages. They wandered from asylum to asylum and ultimately settled at this place Now and then many of them go to their villages to see their children but there they have to stay outside the village

The colony has 45 married couples 67 unmarried men (mostly old) 10 unmarried women and 9 healthy children The ages of the 9 children range from a few days to 4 years.

The colony has a headman and a panchayat elected by the patients from amongst themselves.

Of the previous healthy children in the colony one is in the Patiala army and another is receiving education at Dehra Dun If some arrangement could be made

to separate the healthy children present in the colony, a large number of them are likely to grow into healthy adults and become useful members of the society The parents of the children are willing to give away the children to suitable persons or institutions

The State help —At present no patient gets any help from the State It is said that the monthly amount of Rs 4 sanctioned in 1930 was stopped because the inmates did not stop begging

The religious institutions —The Punjab Khetra and the Kali Kambli Khetra provide free ration to the inmates It is said that Rishikesh has about 2,000 Sadhus and Mahatmas On enquiry I found that no one ever visits the colony to impart religious instructions to the patients

The past history of the patients —The enquiries made from the inmates indicated that a patient of leprosy, whether of the neural or the lepromatous type, in most cases could stay in his village until an ulcer appeared and then he had to go and live outside the village After spending some time outside the village, the patients usually left for other places since they found life less and less comfortable

The Survey

General —The survey was not limited to any one Patti The villages situated near the main road and known to have cases of leprosy were selected for the survey These villages are included in the various Pattis known to be affected with leprosy Forty such villages were visited The findings made are given below

The gross findings —The main findings of the survey are tabulated below —

Population	Cases			Incidence %	Proportion of L cases
	N	L	Total		
7 082	114	28	142	2 05	20%

The findings by Pattis —The findings made in the various Pattis are given in the following table —

Name of Patti	Population	Percentage population examined	Cases			Incidence %	Type distribution Proportion of L cases	Sex distribution Proportion of cases in males.
			N	L	Total			
Nagun	463	30	3	2	5	1 08	40%	80%
Bhandarsu	709	60	12	3	15	2 11	20%	80%
Badkot	1 034	75	15	5	20	1 93	25%	85%
Thakral	2 459	75	35	8	43	1 74	18%	72%
Badiar	525	100	12	1	13	2 47	8%	54%
Ramasaram	991	55	19	5	24	2 42	20%	79%
Mugarsanti	340	65	10	2	12	3 52	17%	75%
Silwar	561	60	8	2	10	1 78	20%	80%
Surveyed area	7 082		114	28	142	2 05	20%	75%

Type and sub-type of the cases —The distribution of the cases into types and sub-types, and the extent of the disease is shown in the following table —

	Na			Ns			Nt			L			
	1	2	3	1	2	3	1	2	3	1	2	3	
Male	7	15	14	14	10	0	22	3	0	5	12	5	107
	1	8	6	5	5	0	3	1	0	1	2	3	35
	8	23	20	19	15	0	25	4	0	6	14	8	142

Of the neuro-anaesthetic cases 31 were classified as Na_1 and Na_2. These cases had only areas of anaesthesia without any deformities or ulcers. These cases constitute 22% of the total cases. In the absence of ulcers deformities and macules these cases are likely to be missed if the examination is not very thorough. In case a majority of them are missed in a survey the proportion of L cases in the area would work out to be very high.

It has often been stated that in the northern hills of India leprosy is virulent and that tuberculoid cases are not found. However amongst the cases found in the present survey 29 or 20% were found to be tuberculoid. In one of these cases the superficial peroneal nerve was as thick as the thumb of the man. Except one none of the lepromatous cases had throat affection. A few had eye affection but none had his eye destroyed. No case of leprotic alopecia was seen.

Type-distribution of the cases by sex and age.—The following table gives the type-distribution of the cases by sex and age —

	Neural			Lepromatous.			Total.	Proportion of cases in the age group.
	Male	Female	Total	Male	Female	Total.		
0–14	4	2	6	0	0	0	6	4·2%
15–34	21	9	30	9	3	12	42	29·5%
35 and over	60	18	78	13	3	16	94	66·1%
	85	29	114	22	6	28	142	99·8%

The proportion of cases in children is very low (4·2%) and no lepromatous cases have been found in them. The age group 15–34 is responsible for about 30% of the cases and about one third of these are lepromatous. The age group 35 and over is responsible for the largest proportion of the cases (66%) but only about one-sixth of these cases are lepromatous.

The village isolation seen during the survey.—Eleven neural and five lepromatous cases were seen isolated outside the villages. The neural cases were mostly Na_3 ones. Out of the 8 Pattis visited isolation was practised in 3 Pattis. In the higher hills and in the ravine isolation does not seem to be in vogue.

Suggestions

The development of the colony.—With the limited resources available the most profitable line of work appears to be the development of the colony at Mumkirti. The conditions at the colony should be made more attractive and proper arrangements should be made for the treatment of patients. As far as possible only infectious cases should be admitted. The colony should serve the whole State but special efforts should be made to bring all the infectious cases from at least one Patti so that in time it may be possible to demonstrate the effectiveness of isolation as a method to control the spread of the disease in a locality.

The staff at the colony.—A medical man trained in leprosy work should be in charge of the colony. It may be necessary to select a person for the job and have him trained. One of the duties of the officer may be to tour in the State and find out suitable cases for admission to the colony. This will necessitate the provision of an assistant who can carry on the work in the absence of the officer in charge on tour. The assistant should also be trained in leprosy work.

Trained injectors and dressers shall be needed. Among the present patients at the colony there are some who have worked as injectors and dressers in leper asylums for several years. These persons can be employed to do the jobs, and should be paid for their services.

For the sake of maintaining discipline and of preventing the patients from going out for begging it may be necessary to employ a few of the inmates as special policemen. When this is done the existing public nuisance will be removed and charities in various shapes can be expected from rich pilgrims.

Maintenance of the inmates —With the help available from the two Khetras, it will not cost the State much to look after the patients It is advisable to make some regular arrangements with these Khetras

Buildings and equipment, etc —It will be necessary to build a dispensary and a small ward for patients needing indoor treatment Quarters for the patients can gradually be built The superintendent and his assistant can stay either at Rishikesh or Mumkirti Syringes and drugs for injections have to be purchased

The cost of the above scheme —The following is a rough estimate of the cost (based on normal pre-war rates) of putting the above suggestion into action —

	Rs
Non-recurring expenses—	
Dispensary and Ward	1,000
Equipment	400
Training of the Supdt	300
Improvement of the water supply	300
TOTAL	2,000
Recurring expenses for 200 patients—	
Clothes @ Rs 6 per year per patient 200×6	1,200
Allowance for dal and vegetables (other ration to be supplied by the Khetras) @ Rs 2 per month 200×2×12	4,800
Allowance of two injectors (patients) 10×2×12	240
Allowance of one dresser (patient) 8×12	96
Allowance of two policemen (patients) 5×2×12	120
Medicine, etc	400
Allowance to Medical Officer 100×12	1,200
Assistant 25×12	300
Building of cottages and repair to existing ones	600
TOTAL	8,956

An Advisory Committee —In the interest of the working of the colony it would be advisable to have an advisory committee with representatives from local public and religious and social organisations This would stimulate public interest and will be instrumental in getting increasing amount of moral and financial support from the people The scope of the colony may in this way be greatly extended without any additional cost to the State

ABSTRACT FROM CURRENT LITERATURE

An investigation of the effects of Cocoyam on leprosy by T F Davey and C M Ross *Lep Rev*, Vol XV, p 3

Oberdoerffer had suggested that a diet rich in cocoyam may predispose persons to leprosy This action of cocoyam was attributed to a sapotoxin which has a specific action primarily on the adrenal glands The authors have investigated this matter by studying the effect of massive doses of cocoyam given to a group of children suffering from leprosy

Twenty-eight children were selected representing all the main types of leprosy (Group I) An equal number of controls was selected comparable in age, type and extent of the disease with those of Group I (Group II) All the children in both the groups were subjected to detailed observations from one cocoyam season to the next, and their progress was followed throughout the year

From March 1st, 1940, when the experiment commenced, until June 30th, children in Group I, in addition to their normal diet, were given massive

doses of cocoyam daily the average daily amount being 2 lbs of prepared cocoyam per child. The supply of cocoyam had to be stopped at the end of June as the cocoyam season was then over, and the tubers were unobtainable No cocoyam was given to the children in Group II Both the groups were kept under observation for one year up to March 1941 Throughout this period no leprosy treatment whatsoever was given The children in both groups were examined daily, weights were recorded weekly sedimentation test was carried out fortnightly and thorough bacteriological tests were carried out at least once a month. A detailed record was thus obtained of the progress of the children in both groups over a period of one year the only difference between the groups being that those in Group I received the massive doses of cocoyam for four months of the year

The progress of the children in the two groups showed that the children in Group I suffered from no ill effects from the cocoyam consumed as a matter of fact their progress compared favourably with that of children in Group II to whom no cocoyam was given

The cocoyam used in the experiment was boiled before being given to the patients This is the usual method which the local people employ It is possible that sapotoxin is destroyed by heat and the method of preparation of the cocoyam destroys the sapotoxin. If the sapotoxin is destroyed by heat the intake of cocoyam is not likely to be of much importance since it is never eaten in an uncooked state the uncooked tubers having an unpleasant acrid taste The authors do not consider the results of their investigation to be conclusive but state that after providing and exaggerating the conditions of life favourable to the exhibition of specific toxic effect by the sapotoxin of cocoyam, they could not trace any deleterious effects in leprosy The authors summarise their article as under —

1 In order to investigate the action of the sapotoxin of cocoyam on leprosy and thereby estimate its importance as a predisposing agent in infection with leprosy a group of children suffering from leprosy were fed with massive doses of cocoyam. Cases with low resistance were selected in order to provide conditions most suitable for the exhibition of the toxic effects of the sapotoxin. The children together with an equal number of controls, were subjected to detailed observation for one year
2 No deleterious effects whatever could be observed.
3 Possible fallacies are dealt with and a wider discussion on questions of diet and seasonal variations of appearances of leprosy leads to the conclusion that although the sapotoxin may possibly exert some slight toxic effect in actual living condition this action is not specific and the sapotoxin is but one among many factors predisposing to infection with leprosy in Nigeria.

REPORTS

LEPROSY SURVEYS IN HYDERABAD DECCAN*

By A. SHAMA RAO *Leprosy Officer*

INTRODUCTION

The surveys were carried out in the villages lying within a radius of 5 miles from the existing leprosy clinics attached to the hospitals or dispensaries. House to house visits and clinical examination of cases and their contacts were made. The advantages of treatment of early cases and the importance of isolation of infectious cases were impressed upon the public. Printed handbills were distributed

* In 1943 the Hyderabad Government sanctioned a scheme of carrying out a leprosy survey in the State over a period of two years. Selected areas in 9 out of the 17 districts in the State have already been surveyed and the work in the other districts is in progress. Report on the survey findings in 5 districts appeared in our January 1944 issue The findings made in the other 4 districts are abstracted here.—*Editor Leprosy in India.*

explaining the nature of leprosy, its early signs and symptoms, and the methods of prevention and isolation. Magic lantern lectures were given in the villages

The findings in the different districts will first be given district by district and then the main findings made in all the districts will be summarised

KARIMNAGAR DISTRICT

Gross findings

No of villages	Area	Total population	Cases detected			Percentage of L cases	Incidence %
			N	L	Total		
36	200 sq miles	48,818	91	28	119	23 53	0 24

Type, age and sex distribution of cases

Age group	Cases									Percentage of L cases	Percentage in age group
	N			L			Total for age groups				
	M	F	Total	M	F	Total	M	F	Total		
0–14	9	2	11				9	2	11	0 0	9 24
15–34	16	9	25	8		8	24	9	33	24·24	27 73
Over 34	40	15	55	15	5	20	55	20	75	26 67	63 03
Total	65	26	91	23	5	28	88	31	119	23 53	100%

WARANGAL DISTRICT

Gross incidence

No of villages	Area.	Total population	Cases detected			Percentage of L cases	Incidence %
			N	L	Total		
12	75 sq miles.	16 860	27	24	51	47 06	0 30

Type, age and sex distribution of cases

Age group	Cases									Percentage of L cases	Percentage in age group
	N			L			Total for age groups				
	M	F	Total	M	F	Total	M	F	Total		
0–14	2	2	4				2	2	4	0 0	7 84
15–34	5	8	13	10	2	12	15	10	25	48 00	49 02
Over 34	7	3	10	10	2	12	17	5	22	54 54	43 14
Total	14	13	27	20	4	24	34	17	51	47 06	100%

ADILABAD DISTRICT

Gross findings

No of villages	Area.	Total population	Cases detected.			Percentage of L cases	Incidence %
			N	L	Total		
[illegible]	200 sq miles	26 893	59	23	82	28 05	0 30

Type age and sex distribution of cases

Age group	Cases.									Per centage of L cases	Per centage in age group
	N			L			Total for age groups.				
	M	F	Total	M	F	Total	M	F	Total		
0–14	6		6				6		6		7 32
15–34	9	9	18	4	1	5	13	10	23	21 74	28·05
Over 34	25	10	35	16	2	18	41	12	53	35·96	64·65
Total	40	19	59	20	3	23	60	22	82	28·05	100%

Nanded District

Gross findings

No of villages.	Area.	Total population	Cases detected.			Percentage of L cases	Incidence %
			N	L	Total		
48	200 sq miles	21 952	58	23	81	28 39	0·36

Type age and sex distribution of cases

Age group	Cases.									Per centage of L cases.	Per centage in age group
	N			L			Total for age groups.				
	M	F	Total	M	F	Total	M	F	Total		
0–14	2	5	7				2	5	7		8 64
15–34	15	2	17	11	1	12	26	3	29	41 37	35 80
Over 34	22	12	34	7	4	11	29	16	45	24 44	55 56
Total	39	19	58	18	5	23	57	24	81	28 39	100%

The main findings in all the four districts.

The main findings in all of the four districts are summarised in the following table —

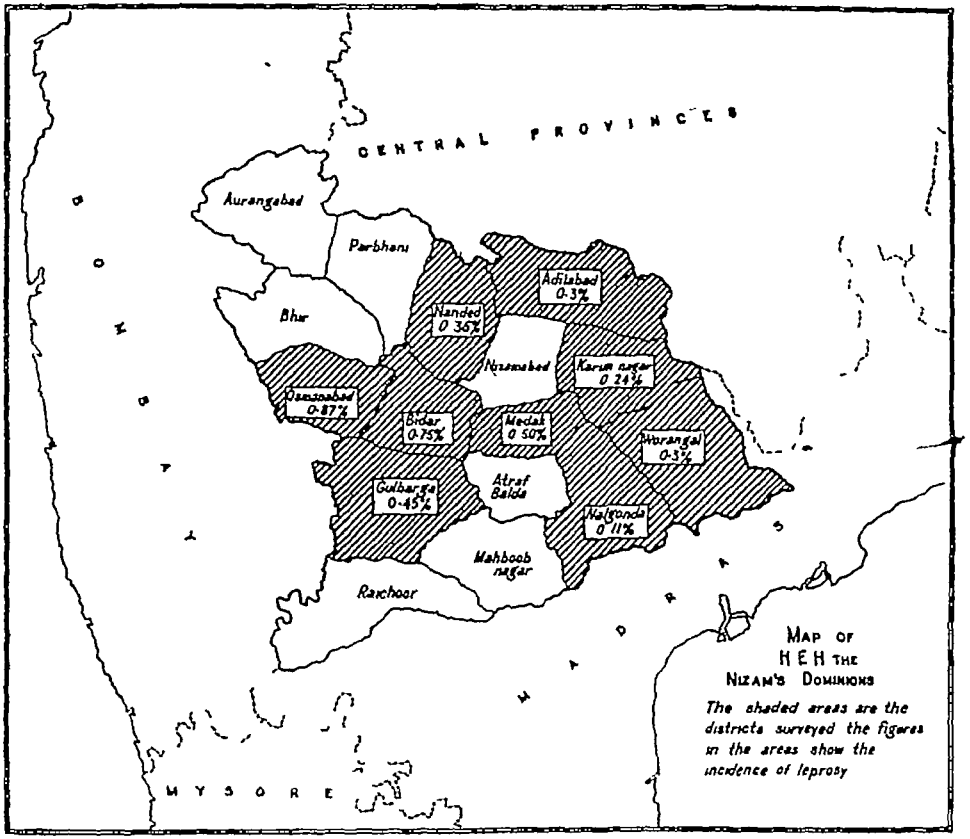
Districts surveyed.	No of villages surveyed.	Total population.	Total No of cases.	Percentage Incidence.	Percentage of L cases.	Percentage in children below 15 years.
Karimnagar	36	48 818	119	0·24	23 53	9·24
Warangal	12	16 860	51	0·30	47·06	7 84
Adilabad	40	26 893	82	0 30	28·05	7 32
Nanded	48	21 952	81	0·36	28 39	8·64

Some comments on the above findings.

Incidence

The incidence of the disease in these districts varies from ·24 to 36% The incidence in these districts is lower than in some of the western districts surveyed (Osmanabad 0·87% Bidar 0·75% and Gulbarga 0·45%)

These survey figures for the incidence of leprosy are from 6 to 30 times higher than the figures reported in the 1931 census for these districts



While leprosy has been found in all castes, the incidence has been highest in the lower castes, such as Dheds, Mangs, Shepherds, and Toddy-tappers

Type distribution

The proportion of lepromatous case varies from 23% in Karimnagar to 47% in Warangal. Thus the percentage of lepromatous cases has been found to be high in all the areas surveyed

Age distribution

The proportion of cases in children below the age of 15 in all the four districts is below 10 Thus in all districts surveyed, the proportion of cases in children is rather low

Sex distribution

Over 70% of the cases detected have been in males, i e the ratio of cases in males and females is about 3 1 *

* These figures cannot be accepted as truly representing the sex incidence of the disease because of the prevalence of males, and the absence of a female to examine the ladies —*Editor in India*

Conclusions

In view of the above findings it is considered that leprosy is not a serious problem in the areas surveyed *

SOME GENERAL INFORMATION ABOUT THE AREAS SURVEYED

The following table gives some general information about the areas —

District	Race	Altitude	Rainfall.	Climate	Isolation of leprosy cases.	Main crop
Karimnagar	Telangana	800–1000	36	Humid	Some home isolation	Rice jowar maize
Warangal	Do	200–400	36	Dry	Do	Rice jowar
Adilabad	Do	400–600	35	Hot and dry in summer Cold in winter	No	Rice jowar maize
Nanded	Marhata wada	400–800	30	Do	Some home isolation	Jowar wheat pulse

Annual Report of the Anti leprosy Work in Ceylon for 1943

The report opens with the remarks that in spite of the difficulties associated with the war condition the anti leprosy work in the Island has been progressing satisfactorily There have been a certain amount of dissatisfaction owing to reduced ration of rice in one of the hospitals during the latter part of the year There were several hostile demonstration against the administration and in one instance even the armed police had to be summoned—

The anti leprosy work in Ceylon includes (1) the maintenance of the two hospitals for segregation and treatment of infectious cases of leprosy (2) the maintenance of 24 outdoor clinics attached to civil hospitals and dispensaries for treatment and observation of non infective cases of leprosy (3) the field organisation for detection of new cases of leprosy etc

The report under review gives a brief outline of the work done during the year on the above lines and is abstracted below

Leprosy hospitals—There are two leprosy hospitals one at Hindola and the other at Montivu. These hospitals are mainly for the segregation and treatment of the infective cases of leprosy but cases of the neural type needing treatment for complications such as ulcers etc are also admitted into these hospitals

At the end of 1942 there were 1 073 cases scheduled in the two hospitals During 1943 there were 137 admissions and 29 re-admissions. During the same period 8 patients were discharged 130 died and 11 were repatriated to India, i.e at the end of 1943 there were 1 090 cases scheduled at these two hospitals Of these 1 090 cases 121 were absconding and 63 had left so that only 806 cases were living at the two hospitals at the end of 1943 The hospitals provided facilities for occupational therapy and educational and recreational activities The facilities for occupational therapy included vegetable gardening animal husbandry and weaving etc. The education department maintains school at both the hospitals recreational activities including shows of cinema and provision of indoor and outdoor games.

Clinics—During the year there were 24 clinics operating in the endemic areas. They are meant for the treatment and observation of non infective cases of leprosy and are attached to civil hospitals and dispensaries During the year 1,472 cases were scheduled to these clinics 389 for treatment and 932 for observation

* The incidence and the proportion of cases in children is not very high yet the proportion of lepromatous cases in all the areas is high We do not consider that the statement that leprosy is not a serious problem in these areas is justifiable.—*Editor Leprosy in India*

Field work—The field work consists of home visits for observation of paroled cases and contacts, examination of schools and leprosy propaganda, etc

During the year 195 fresh cases of leprosy were detected against 180 in 1942, 248 in 1941, 330 in 1940 Of the 195 cases, 64 were amongst contacts of previously known cases of leprosy

Seventeen (8 7%) of the cases were in children below the age of 14. One hundred and fifty eight (81%) of the cases were found amongst the males and 94 (47%) of these cases were of the lepromatous type One hundred and one (53%) were of the neural type

Of the newly detected cases, 76 lepromatous cases have been segregated into hospitals and 18 are waiting for segregation Of the 101 neural cases, 20 have been admitted into the hospital for treatment of ulcers and 81 have been discharged on parole

Present leprosy picture on the Island—The total number of living cases at the end of 1943 was 2,823, 1,090 in hospitals and 1,733 on parole The total living cases at the end of 1942 was 2,857 The report ends with the following conclusion —

> It is encouraging to note that the total number of living cases of leprosy which showed a decrease in number since 1941 has maintained that downward trend in spite of difficult conditions of war poverty malnutrition and rationing of food The whole Island is now under the organised scheme of Leprosy Control Prior to 1941 the new detections were over 350 cases per year but now this number has decreased to about 200 for the year The number amongst children which was over 50 per year for a number of years is now below 20 for the last three years These results are no doubt the result of organised control of leprosy and other Public Health measures

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Report for 1943—Premananda Leper Dispensaries

This is a report of an organisation which runs two leprosy clinics, one at 259 Upper Circular Road, Manicktola and the other at 3-A Nibaran Banerji Road, Kalighat These dispensaries are doing excellent work for leprosy patients amongst both general public and the beggars of the city

The report opens with a reference to the economic distress experienced in the province during 1943, and its effects on the working of the dispensaries The economic distress caused a slight drop in the number of patients and in their attendance During the year 757 new cases were treated at the two clinics Over 1,000 old cases belonging to the middle and working classes of people, and 258 beggar patients attended the two clinics The home visiting work was carried under difficult conditions on account of the food crisis in the city

A batch of girl students from the Sir John Anderson Health School received a short course of training in leprosy for two weeks Special attention was given to the diagnosis of early cases of leprosy

On account of the generosity of the donors it was possible to have the usual Christmas feastings at the Manicktola clinic and at the Albert Victor Hospital, Gobra

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The Annual Reports for 1943 of the Provincial Branches of B E L R A

These reports are here all abstracted

Madras

GENERAL

The Provincial Council is responsible for certain special branches of leprosy work and for the investigation work done in the Presidency, the routine work of leprosy diagnosis and treatment, etc being left to other agencies

Dr R G Cochrane, Chief Medical Officer, Lady Willingdon Leprosy Sanatorium, Chingleput, is the Honorary Secretary of the Madras Provincial Council, and directs the various lines of investigations, but in charge of each investigation unit is a fully trained officer

The Honorary Secretary also advises the Government on the gradual building up of an anti-leprosy scheme which will ultimately cover the whole Presidency Outlines for a scheme for post war reconstruction in leprosy work have been placed before the Government. It is sincerely hoped that the subject will receive increasing attention in the post war world for it cannot be too strongly emphasised that unless leprosy is considered as primarily a medical problem and governments are prepared to spend a great deal of money and encourage men of the highest grade to specialise in the subject no advance will be made and leprosy will remain an unsolved problem.

SPECIAL INVESTIGATIONS.

The work of the Provincial Council is carried out at the following investigation centres —

1 Lady Willingdon Leprosy Sanatorium Chingleput
2 Silver Jubilee Clinic for the Study of Childhood Leprosy Saidapet
3 Rural Leprosy Investigation Centre Polambakkam
4 Urban Leprosy Investigation Centre Madras City
5 Children s Sanatorium Ethapur Salem District.
6 Silver Jubilee Clinic, Madura

The work of these centres is very briefly discussed below —

Lady Willingdon Leprosy Sanatorium Chingleput

Clinical histological immunological and therapeutic studies have been continued in this Sanatorium. The following observations have been made —

Clinical and histological studies —The macules of leprosy can generally be divided histologically into the following four groups —

(*a*) Macules that show indefinite or non-specific histology This group can be subdivided further according to whether or not there is evidence of commencing nerve involvement
(*b*) Macules which show definite tuberculoid histology
(*c*) Macules which show definite lepromatous histology
(*d*) Macules in which the features are not characteristic either of tuberculoid or of lepromatous patches. These macules are included under the term intermediate or border line cases.

These studies have confirmed the opinion previously held that true tuberculoid leprosy does not develop into lepromatous leprosy

A detailed histological study of the lepromatous type of leprosy has been started The study so far made indicates that there may be several sub-types in the lepromatous type

Immunological studies —The work on the lepromin test has been continued refined lepromin obtained from Calcutta or prepared according to the Calcutta method has been used

It is confirmed that the positive lepromin test has a definite relationship to prognosis and that atypical cases usually give atypical results with the lepromin test

A study of the intensity of the reaction confirms the finding of the Calcutta workers that there appears to be a relationship between the severity of the tissue reaction and the lepromin reaction in tuberculoid cases. However there does not appear to be such a correlation ship in cases of the intermediate group

A positive result with the lepromin test has so far not been noticed in a lepromatous case

Therapeutic studies —Work has been continued throughout the year on the trial of some new remedies but so far with completely inconclusive results.

The experiment to discover the optimum dose of the hydnocarpus remedies has been continued but the results are inconclusive

Investigations have been made on the best method of giving injections of the hydnocarpus remedies Three methods were tried (*a*) Only subcutaneous injections, (*b*) only intradermal injections, and (*c*) a combination of intradermal and subcutaneous methods Judging by the number of cases that have become bacteriologically negative in the three groups, it is considered that a combination of the intradermal and subcutaneous methods is better than either method alone This opinion is strengthened by the fact that the average length of treatment in the group treated by a combination of subcutaneous and intradermal injections has been shorter than in the other two groups, although the results have been more satisfactory

Spontaneous arrest in lepromatous cases —It has been stated from time to time that lepromatous leprosy may become spontaneously cured A small series of cases, in which some of the lesions were bacteriologically negative, was taken for study in this connection Amongst the cases receiving treatment, 3 became negative, and 1 worse Amongst the cases not getting any treatment, 2 became negative, and 3 worse This confirms the impression that certain early lepromas may become negative without treatment

Significance of a positive Wassermann test in leprosy —An investigation has been made into the significance of a positive Wassermann test in leprosy Ten lepromatous cases, divided into two groups, have been used for this investigation The Wassermann and Kahn reactions were positive in all the ten cases One group was treated with Avenyl (a mercury preparation recommended by Muir) in hydnocarpus oil, and the other group received only the routine treatment with hydnocarpus oil In the group treated with Avenyl none of the cases became Wassermann or Kahn negative, while in the other group in two cases strongly positive Wassermann and Kahn reactions became negative after treatment The negative results of the Wassermann or Kahn tests corresponded with marked improvement in the clinical and bacteriological conditions This suggests that in these cases leprosy was responsible for the positive Wassermann and Kahn tests

Silver Jubilee Clinic, Saidapet

The work of this centre as in previous years has included epidemiological and clinical investigations Over 700 children are under observation at this centre This centre presents a unique opportunity for the study of the development of lesions of leprosy, and this study is considered to be of utmost importance, for it has a bearing on the epidemiology as well as the progress of the disease

A further analysis of the findings made at this centre supports the impression already gained that the lesions most likely to become lepromatous are the simple macules of the neural leprosy, and the incipient lesions in the children, of the 221 children in the simple neural group 6 33% have become lepromatous during the past seven years, this change has been seen in 33% of children in the incipient group, and in only 1 39% in the tuberculoid group In all these tuberculoid cases the tuberculoid change was of minor degree, and the lepromin test was negative

Of the 118 children kept under observation for having suspicious signs of leprosy 19 have so far developed definite signs of leprosy The study indicates that the first lesion of leprosy is a macule, but that it is not always possible to differentiate such macules from other macules which later do not develop into definite patches of leprosy A study is being made in order to be able to make such a differentiation possible

Rural Leprosy Investigation Centre, Polambakkam

One of the chief aims of this centre is to endeavour to discover a method of control which is practicable in rural areas The experiment with night segregation has been continued It is yet difficult to come to a definite conclusion regarding the efficacy of night segregation However, it is of interest to note that in the village where all the infective patients are completely or partly segregated no child cases or an infective case has arisen in the last 18 months

Children s Sanatorium Etahpur Salem

There are now 49 children in the Sanatorium, and the work is being gradually developed.

Silver Jubilee Clinic Madura

The work at this clinic has continued. The clinic has become more popular because of the facilities for treating emergency cases as indoor patients.

TEACHING

Two special training courses each of a fortnight s duration were held during the year in the Lady Willingdon Leprosy Sanatorium, and were attended by 19 doctors. An examination was held at the end of each course and the successful candidates were granted certificates. The results of the examination tend to indicate that possibly there is a need for two kinds of courses a preliminary course for the beginners and a more advanced course for persons having some previous experience of the disease

An outstanding development during the year has been the establishment of leprosy departments in the teaching hospitals. The Leprosy Department of the General Hospitals Madras is fully organised and it is hoped to complete during this year the organisation of the leprosy departments at the Stanley Medical College Hospital Royapuram Madras and the King George s Hospital, Vizagapatam.

FINANCES.

The receipts during the year amounted to a little over Rs 27 000 and the expenses to about Rs.31 000 The income of the Branch consists mostly of grants from the Madras Government (Rs.21 500) the Indian Council of B.E.L R A. (Rs.3 200) and Madras City Branch (Rs 1 500) In addition over Rs.1 000 were collected as donations. About Rs.5 000 each were spent on expenses in connection with the Head Office Madras City Urban Leprosy Investigation Centre Silver Jubilee Clinic Saidapet and on the salaries of the Group Investigation Officers. Over Rs.11 000 were spent on the Children s Sanatorium Etahpur

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Bengal

GENERAL.

In Bengal anti-leprosy work is done largely by the District Boards and Municipalities The policy of the Bengal Branch of B E.L R.A. has been to co-operate with the District Boards and the Municipalities and to encourage the development of anti leprosy work done by these bodies by offering free services of their staff The staff of the Branch consists of one Leprosy Officer three Assistant Leprosy Officers and one Publicity Officer

During the year the anti leprosy work has been continued on these lines. Later in the year however the famine developed in Bengal and in these emergency conditions it was thought that the staff of the Branch should devote themselves for the time being entirely to the relief work.

TREATMENT

The District Boards and the Municipalities are responsible for the establishment and maintenance of a large number of clinics in Bengal. The Provincial Branch helps by arranging inspection of these clinics by their staff who make necessary suggestions for improvement in the work.

During the year visits were paid by the staff to 17 leprosy clinics in different parts of the province The work of the clinics was examined and the medical staff

were advised regarding the work, and recommendations were sent to the local authorities concerned regarding the running of these clinics

Surveys

During the year surveys of small areas in five districts of Bengal were made, and a total population of over 30,000 was examined The findings made in these surveys are summarised in the following table —

Area.	Total population	No Exd	Cases detected	Incidence	Age distribution Proportion cases in children under 15	Type distribution Proportion L cases
Hirapur Mouza, P S Burnpur (Dist Burdwan)	2 882	2,155	62	2 1%	34%	22 6%
Round Tanore Leprosy Clinic (Rajshahi Dist)	5,212	4 081	20	5%	20%	15%
Selected areas in Bhatpara Municipality (24-Pargs Dist)	9 500	7 215	106	1 5%	10%	14%
Amta P S (Howrah Dist)	7,506	5 831	30	5%	Nil	38 3%
Domjur P S (Howrah Dist)	4,318	3,395	14	4%	14 3%	21 4%

The work started during 1942 on the study of leprosy in the general population of Calcutta was continued during 1943 The following conclusions have been based on this study —

(1) That there is a large number of patients with leprosy living within the city of Calcutta
(2) That most of these patients are not leper beggars who have migrated to the city but are part of the permanent population of Calcutta
(3) That many of them are infected in Calcutta
(4) That most of them, as long as they are able to do so, continue to follow their occupations in Calcutta

Work in the Schools

During the year the work in the schools included the examination of school children for leprosy, and teaching of the school children about leprosy This work was done in about 100 schools in different parts of the province Some cases of leprosy were detected in the schools, and recommendations regarding the treatment and management of these cases were given to the school authorities

Propaganda

Since the services of the Publicity Officer, early in the year, were lent to the Blood Bank, very little propaganda work had been done during the year except that done in connection with the surveys and the work in the schools

Isolation

During the year the Silda Peddie Leprosy Clinic in the Midnapore District has established an isolation colony for infectious cases in Bhairabdanga There is accommodation for 12 patients, and the place has always been full since it was opened In spite of famine conditions it has been possible to obtain chiefly by local collections, sufficient rice to feed the inmates, and sufficient money to pay four annas per week

to each inmate The Bengal B.E.L R.A. made a non recurring contribution of Rs.500 for the establishment of this colony

TRAINING

Thirteen doctors deputed by local authorities in Bengal attended a fortnight s course on leprosy in the Leprosy Department of the School of Tropical Medicine from the 17th to 29th May 1943 Ten of the 13 passed the examination at the end of the course

During the year courses of lectures on leprosy were given in the Burdwan Medical School and the Calcutta Medical School.

FINANCES.

The receipts during the year amounted to about Rs 16 800 Rs 10 000 from the Bengal Government Rs 1 480 from the Calcutta Corporation Rs.1 000 from the Crichton Trust Rs 2 000 from the Indian Council of B E L R.A about Rs.1 000 from the District Boards and Municipalities and Rs.500 as donation from His Excellency the Governor of Bengal. The total expenditure during the year has been about Rs 18 500

Bombay

GENERAL.

The main activities of the Provincial Council consist in carrying out leprosy surveys doing leprosy propaganda and training the medical officers in the diagnosis and treatment of leprosy The following agencies are engaged in the anti leprosy work in the Presidency —

The Medical Department of the Provincial Government
The Provincial Council of B E.L R A.
Mission to Lepers
Municipalities and Local Boards etc

The Medical Department of the Provincial Government gives grants-in aid to the leprosy institutions in the Presidency and maintains a leprosy hospital and a Provincial Leprosy Officer The Public Health Department of the Provincial Government does not take any part in the anti leprosy activities in the province The Bombay Municipality maintains the biggest leprosy institution in the province the Ackworth Leper Home Matunga Bombay In addition, there are three institutions maintained by voluntary organisations or local bodies.

The Provincial Leprosy Officer employed by the Government resigned during the year and this vacancy has not yet been filled because of the lack of a suitable candidate The duties of the Provincial Leprosy Officer are to carry out surveys in the different parts of the Presidency to supervise the work of the District Councils and to help in the organisation of such Councils in those districts where they do not exist.

TREATMENT

There are no special leprosy clinics except the one at the Ackworth Leper Home There are 42 centres scattered all over the Presidency where treatment for leprosy is given. Cases of leprosy are also treated in many Government dispensaries. The number of such Government dispensaries has been 86 during 1943 against 80 in 1942

At the 42 centres 4,821 cases attended for treatment 3 168 old cases and 1 653 new cases. Of the cases attending for treatment nearly 50% were of the neural type and the other 50% of the lepromatous type

The total number of patients treated during the year at the Government dispensaries was 1 660 against 1 830 in 1942

INSTITUTIONS

The following is a list of the Leper Homes and Hospitals, etc in the Presidency —

		Location	*Run by*
1	The Ackworth Leper Home	Matunga	Bombay Municipality
2	Leper Hospital	Vengurla	Mission
3	F E Albless Leper Home	Trombay, Bombay	Private body
4	Leper Hospital	Ratnagiri	Government
5	do	Nasik	Mission
6	do	Poladpur	do
7	do	Sholapur	District Leprosy Council
8	do	Belgaum	Mission to Lepers
9	do	Khondwa	Government
10	do	Miraj	Mission
11	do	Kagrapeth, Ahmedabad	Government
12	do	Surat	Partly aided by Government
13	do	Sankheshwar	Mission
14	do	Bijapur	District Leprosy Council

SURVEYS

The Provincial Leprosy Officer carried out rough surveys of Type I (according to the Leprosy Survey Sub-Committee's Report of the Indian Research Fund Association) in 13 districts One hundred and fifty villages with a total population of about three lakhs were surveyed, on an average 14% of the population was examined. Six hundred and eighty-four cases of leprosy were detected The incidence of the disease in the various districts surveyed is given below —

District	*Incidence %*
Sholapur	53
East Khandesh	53
Ratnagiri	23
Nasik	28
Ahmednagar	22
Poona	16
Bijapur	17
Satara	6
West Khandesh	19
Ahmedabad	01
Kaira	01
Surat	11
Broach and Panch Mahals	1

PROPAGANDA

The propaganda work consisted of lectures or lantern slide demonstrations, and instructions for taking early treatment

TRAINING

The Ackworth Leper Home conducts two courses of training every year—one, a short course of a fortnight's duration, and the other, an extended course of three months' duration During 1943, four officers attended the three months' course, eight the fortnight's course

FINANCES

The year opened with a balance of Rs 10 739-5-0 An amount of Rs.13,487-8-0 was received during the year as contribution from the headquarters. An amount of Rs.14 253 10-0 was spent on the maintenance of treatment centres in the Province The year closed with a balance of Rs 9 973 3-0

Orissa

GENERAL.

The Executive Committee of the Provincial Council of the British Empire Leprosy Relief Association is composed of both official and non-official members with the Director of Health and Inspector General of Prisons Orissa as its *ex-officio* Chairman. The Association employs 7 District Leprosy Relief Officers 29 Leprosy Assistants and 6 Lady Assistants to carry on mainly the survey and propaganda work. It also maintains 29 leprosy clinics in suitable places in the interior of districts for giving treatment to cases of leprosy A Provincial Leprosy Officer has been maintained by the Provincial Government since 1938 The work of this officer is to supervise and co-ordinate the work of the district leprosy staff appointed by the Provincial Branch, to inspect the clinics and to advise the Executive Committee on the technical aspects of the anti leprosy work in the province

TREATMENT

There are 166 leprosy clinics in the province under the management of the various bodies as detailed below —

Maintained by District authorities and Municipalities	102
Government	29
Provincial Leprosy Relief Association	26
private bodies	9
TOTAL	166

INSTITUTIONS.

The following are the leper hospitals isolation colonies and village isolation centres —

	Accommodation	*Managed by*
Hospitals—		
Cuttack	305	Mission to Lepers
Puri	80	Local Committee
Leper Colonies—		
Lati (Ganjam)	32	District Council Ganjam.
Junani (Sambalpur)	30	District Leprosy Council
Village Isolation Centres—		
Baragarh (Sambalpur)	7	Local Committee
Janla (Puri)	5	Local Leprosy Relief Committee
Chitalo (Cuttack)	8	Do

SURVEYS

Sample surveys in certain areas were carried out by the District Leprosy Officers during the year under report. Sixteen centres having 199 villages were surveyed and 692 cases were detected amongst a total population of 91 000

Central Provinces and Berar

GENERAL

The Provincial Branch of B E L R A consists of a committee with the Director of Public Health as its Hony Secretary The following agencies are engaged in the anti-leprosy work in the province —

The Provincial Government
The Provincial Branch of the B E L R A
Mission to Lepers
Local organisations such as Maharogi Seva Mandal, Wardha, Kashikhed Village Uplift Committee, Raipur Leper Home Committee

The Provincial Government is maintaining a Leprosy Specialist, is running 20 special leprosy clinics and about 35 leprosy clinics attached to hospitals and dispensaries, and is giving grants-in-aid to the leprosy institutions in the province The Provincial Branch of the B E L R A maintains six leprosy clinics similar to those run by the Provincial Government The Mission to Lepers is maintaining six leprosy in-patient institutions with a total accommodation for about 2,000 patients The Maharogi Seva Mandal, Wardha, is running three leprosy clinics and has recently started an in-patient institution The Village Uplift Committee, Kashikhed, has recently started a small colony for the isolation of cases At Raipur a local committee is running a leper home

TREATMENT

There are 25 special leprosy clinics, and 62 sub-centres for treatment attached to these special clinics In addition, 35 leprosy clinics are run in association with the dispensaries in the province Over 6,000 cases of leprosy were treated at these clinics during 1943 Of these over 4,000 were of the neural type, and over 2,000 of the lepromatous type

INSTITUTIONS

There are nine in-patient institutions in the province A list of these institutions with the number of inmates is given below —

Place of the institution	By whom run	Number of inmates
Champa	Mission to Lepers	550
Chandkuri	Do	554
Dhamtari	Do	418
Ellichpur	Do	285
Jhargaon (Mungeli)	Do	88
Rajnandgaon	Do	78
Raipur	Local body	120
Sanhawachhapar	Mr Elvin	26
Duttapur	Maharogi Seva Mandal	20

About 40% of the cases in the institutions are the crippled and non-infective cases It is, however, hoped that in future the admission into these institutions will be restricted to infective cases only

SURVEYS

One Sub-Assistant Health Officer from the Leprosy Section was deputed to Bhandara District for the survey work He has worked in three Police Station House Circles in the Bhandara Tehsil, and has reported a gross incidence of the disease varying from 14% to 34%

In addition, re-surveys carried out by the Sub-Assistant Health Officers on leprosy duty in 24 areas have revealed 677 new cases of leprosy, 158 in the immediate contacts of previous cases

PROPAGANDA

The propaganda is done by the Sub-Assistant Health Officers on leprosy duty and on epidemic duty in the course of their tours in their respective areas Propaganda is also done in exhibitions and fairs etc.

ISOLATION

The question of isolation of infectious cases is receiving increasing attention and attempts are being made to encourage isolation in village isolation centres and small colonies A small colony has been started at Kashikhed by the Village Uplift Board. At present it has only four inmates. The work of this colony has not developed as expected since the Sub-Assistant Health Officer in charge of this colony has left to join the army

TRAINING

Short courses of training in leprosy of one week s duration were held by the Provincial Leprosy Officer at Yeotamal Akola Buldana Saugor Chhindwara Wardha and Raipur Sixty three Assistant Medical Officers and Assistant Surgeons of the various Government dispensaries 34 Sub-Assistant Health Officers of the Public Health Department and 16 private medical practitioners attended these courses

FINANCES.

A sum of Rs 8 700 was received from the Indian Council of B E.L R A. The total expenditure during the year has been Rs 9 400 Of this Rs.8 700 have been spent on the maintenance of the six leprosy clinics and Rs.400 in a grant paid to the Maharogi Seva Mandal, Wardha the balance of Rs 300 has been spent on various items.

Punjab

GENERAL.

The Punjab Branch of B E L R A. consists of a Technical Committee of eleven members all nominated by the Provincial Government. The Inspector General of Civil Hospitals Punjab is the Chairman of the Committee and the Director of Public Health Punjab the Hony Secretary The Committee gives advice and financial assistance to other agencies doing anti leprosy work in the province and maintains the District Leprosy Officer for Kangra and an Assistant Leprosy Officer The Public Health Department Punjab maintains a Provincial Leprosy Officer

The main duties of the Provincial Leprosy Officer consist in carrying out leprosy surveys in the various parts of the province organising and inspecting leprosy clinics and leper homes training medical officers of the various leprosy clinics and giving lecture-demonstrations to the final year students of the various medical institutions of the province The District Leprosy Officer Kangra is responsible for the anti leprosy work in the district excluding Kulu Sub-division and for training the medical officers of the district He also acts as the medical officer Leper Home Palampur Anti-leprosy work in Kulu Sub-division is carried out by the Assistant Leprosy Officer

TREATMENT

The total number of leprosy clinics at the close of 1942 was 195 The leprosy clinic at Bhuntar which had been closed in 1942 was revived during this year Thus the total number of clinics at the end of 1943 was 196 Of these 2 are run by the B E.L R.A Punjab Branch 5 are attached to the leper homes 30 are attached to the dispensaries under the control of the Public Health Department and the remaining 159 are attached to the dispensaries run by the Medical Department.

The attendance at these out patient clinics was extremely irregular and unsatisfactory Of the total number of 1 983 patients on the register at these clinics

only about 900 attended for treatment To rectify this unsatisfactory state of affairs the District Leprosy Officer, Kangra, and the Assistant Leprosy Officer, Kulu, made frequent visits to the clinics during which they discussed the matter with the medical officers, and also got in touch with the patients In addition, full use was made of the staff of the Public Health Department in the rural areas, and of the missionary and other social organisations to persuade the cases to attend the clinics for regular treatment

INSTITUTIONS

There are five leper homes in the province situated at Ambala, Sabathu, Palampur, Tarn Taran and Rawalpindi These homes are run by the various missionary organisations During the year the Punjab Government contributed a sum of Rs 63,700 to these institutions on a *per capita* basis

SURVEYS

Owing to paucity of staff survey work was undertaken only in a limited area The Provincial Leprosy Officer started a survey of Chunian Tehsil in Lahore District The survey is intended to be a Type II survey as described in the report of the Leprosy Survey Sub-Committee of the I R F A Seventy-one villages of the Chunian Tehsil are included in this survey which is still continuing A report will be submitted when the survey has been completed

During the year the District Leprosy Officer, Kangra, and the Assistant Leprosy Officer, Kulu, visited 161 villages and detected 61 new cases of leprosy—19 lepromatous, 23 neural and the rest of doubtful classification

TRAINING

During the year no training course was held The Provincial Leprosy Officer, as usual, gave short courses of lecture-demonstrations to the final year students of the King Edward Medical College, Lahore, the Medical School, Amritsar, and the Women's Christian Medical College, Ludhiana

PROPAGANDA

Anti-leprosy propaganda was carried out by the Provincial Leprosy Officer, the District Leprosy Officer, Kangra, and the Assistant Leprosy Officer, Kulu, during the course of surveys and visits to villages

ISOLATION

The question of isolation of infectious cases is receiving increasing attention The Director of Health, Punjab, has suggested to the Technical Committee of the Punjab B E L R A a scheme for the establishment of a colony for infectious cases of leprosy in the Punjab The Technical Committee has appointed a small sub-committee to examine the scheme in detail, and to submit a report for consideration by the Technical Committee at their next meeting

RESEARCH

The Provincial Leprosy Officer collaborated with Dr Dharmendra of the School of Tropical Medicine, Calcutta, in carrying out immunological studies in the province

FINANCES

About Rs 12,000 was received during the year, over Rs 9,000 from the Indian Council of the B E L R A and the rest from local bodies The total expenditure during the year, excluding the pay and travelling allowances of the Provincial Leprosy Officer which are met by the Government, was Rs 8,500

United Provinces

GENERAL

The main activities of this Branch consist in maintaining three leprosy clinics and a Provincial Leprosy Officer The duties of the Provincial Leprosy Officer are to do survey and propaganda work in the villages and to start treatment centres.

TREATMENT

The Branch continues to maintain the three clinics at Benares Cawnpore and Lucknow The Lucknow clinic continued to voluntarily decrease its demands by 10% annually and it is expected that by the year 1945 this clinic will not require any financial help from the Provincial Branch. The funds thus released could be diverted towards anti leprosy work in some other districts

At the Benares clinic 216 cases received treatment 152 of these were new cases and 64 old cases At Cawnpore the number of the newly enlisted cases during the year was 154 against 144 for the last year At Lucknow the number of cases attending for treatment was 318

All the modern methods of treatment were used including injections of creosoted hydnocarpus oil injections of P.A.T and calcium for reacting cases and of vitamin B_1 for nerve pain etc

SURVEYS

During the year the Provincial Leprosy Officer worked in the district of Sitapur The survey in this district was carried on with the idea of feeding the outdoor leprosy clinics of the Sadar and of the district hospitals with as many new patients as possible Two hundred and sixty two villages were visited and 236 patients were advised and persuaded to take the treatment.

PROPAGANDA

There is lack of suitable propaganda material Lectures in Hindustani were delivered to villagers collected at village meetings. The Nimsar and Hargaon melas were also attended and five cases were detected in these melas.

TRAINING

During the year the Provincial Leprosy Officer trained the medical officers of seven dispensaries two medical officers who came to Sadar dispensaries for the refresher course and three private practitioners

FINANCES.

The Branch received Rs.8 450 from the Indian Council of the B E.L R.A. and spent Rs 6 900 during the year on grants to the three clinics a small non recurring grant to Almorah District Leprosy Relief Council and on salary and travelling expenses of the Provincial Leprosy Relief Officer

Leprosy in India

Vol XXII *October 1950* *No 4*

EDITORIAL NOTES

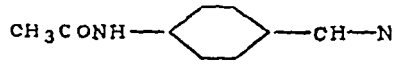
THIOSEMICARBAZONE IN THE TREATMENT OF LEPROSY

The chemotherapeutic agents that have so far held promise in the treatment of tuberculosis are sulphones streptomycin and para amino-salicylic acid (PAS) Recently a new group of sulphur containing compounds has been developed and successfully used in Germany These drugs are known by the general name of *thiosemicarbazones'* and have been extensively used in Germany and of late are being widely tested in the United States and the United Kingdom

The successful use of a remedy in tuberculosis has its implications in the field of the sister disease leprosy and is often instrumental in stimulating research in the treatment of leprosy This approach is necessitated because of the limitations imposed on leprosy workers by the non-cultivation of the leprosy bacillus and the absence of a susceptible laboratory animal Moreover this approach has already been amply justified by being responsible for the introduction of sulphone drugs in the treatment of leprosy an event which has marked a remarkable advance in the therapeutics of this disease

It was therefore natural that the successful use of thiosemicarbazone in the treatment of tuberculosis should arouse interest amongst leprosy workers An editorial on the subject appeared in a recent issue of *International Journal of Leprosy* (Editorial 1950) in which also appear lengthy abstracts of some important articles bearing on the subject published in the January 1950 issue of the *American Review of Tuberculosis* The drug has already been put to trial in the treatment of leprosy by an experienced leprologist, Dr Gordon Ryrie In a preliminary report Ryrie (1950) records promising results in 10 cases of leprosy treated over a period of 4 months all the patients improved clinically and showed bacteriological improvement Ryrie admits that the value of a drug cannot be assessed after such a short period of treatment in a small number of cases all the same he is of the opinion that improvement has been more rapid than would have been possible under the sulphone drugs and that the drug is less toxic than the sulphones These results have certainly made a strong case for an extensive trial of thiosemicarbazone in the treatment of leprosy

These compounds were developed by Domagk in collaboration with workers of the Farbenfabriken Bayer Laboratories at Elberfeld Sulphonamides, sulphones and sulphathiazoles were all found to exert limited anti-tuberculosis activity, but it was found that the activity was not dependent upon the presence of sulphonamide or sulphone groups, nor upon the thiazole or thiadiazole rings, but that an open chain-like arrangement of the nitrogen and sulphur atoms, such as is present in the thiosemicarbazones, represents a much more active basic principle Behnisch, Mietzsch and Schmidt (1950) prepared a large number of compounds containing this principle and found that 4-acetylaminobenzaldehyde-thiosemicarbazone was the most effective preparation This substance is represented by the formula



This product is a pale-yellow finely-crystalline powder of bitter taste, almost insoluble in water, slightly more soluble in serum, and much more soluble in urine Bayer has placed it on the market under the trade name of 'Conteben' It is now being prepared by other laboratories under the proprietary names of 'Tibione' (Schenley Laboratory), 'Myrizone' (Squibb and Sons) and Thiacetazone (Boots) An Indian firm is also producing it under the provisional name of 'PAABT'

Levaditi (1949) and Domagk (1950) have investigated the anti-*tuberculosis activity of Conteben in experimental tuberculosis in animals* In the mice, Levaditi found its effects comparable to that of PAS though inferior to that of streptomycin In guinea-pigs, however, Domagk reported that it was 100 times as active as PAS, and that its activity was of the same order as of streptomycin Besides inhibiting the growth of the tubercle bacillus, Conteben produces morphological changes as also changes in the staining properties, the bacilli first losing their acid-fastness, and later gram-positiveness

The mode of action of Conteben is not definitely known but Domagk believes that it possibly acts directly on the tuberculosis bacillus rather than through some indirect action via the host In common with streptomycin the activity of Conteben is not inhibited by para-amino-benzoic acid, this is in contrast to para-amino-salicylic acid and sulphonamides, the activity of which is inhibited by para-amino-benzoic acid Domagk believes that Conteben has a different mode of action than streptomycin, and that a combination of these two is likely to be more effective than either drug alone

Conteben has been put to extensive clinical trials in Germany, over 10,000 patients with different forms and stages of tuberculosis have been treated and over 60 reports have been published or are under publication The results have been reviewed by Mertens and Bunge (1950) Hinshaw and McDermott (1950) visited Germany and carried out a special survey of the clinical use of Conteben in German centres, these two pioneer workers in the field of chemotherapy of tuberculosis have corroborated the findings reported by German authors on almost all essential points The most marked results are seen in tuberculosis of the mucous membranes, such as tuberculous laryngitis in tuberculosis of the skin and in intestinal tuberculosis, in pulmonary tuberculosis it is the fresh exudative, non-active type of the disease that responds well to this drug

The dose of Conteben is extremely small starting with a small initial dose of 12 5 to 25 mg it is gradually increased and in general the upper limit is considered to be 200 mg per day There are however marked individual variations and the daily dose may have to be smaller still. The principle that the highest dose should be reached as quickly as possible so that high blood levels are obtained as rapidly as possible does not apply to Conteben therapy

The drug is usually given by mouth but it is effective both orally and parenterally Although it is slightly soluble in water it can be rendered suitable for injection by means of solubilizing agents, like antipyrin or by solution in glycols or other suitable substances

At the beginning of the clinical trials with Conteben large doses were used, and untoward toxic symptoms were frequently encountered However with smaller doses in use at present the common toxic symptoms are lack of appetite gastric complications nausea and occasional vomiting These symptoms disappear as the treatment is continued The patients may occasionally complain of dizziness and conjunctivitis and dermatitis may occasionally be seen On the present dosage anæmia is said to be relatively rare

* * * * *

It would appear that thiosemicarbazone has opened a new and fruitful field for therapeutic investigations in leprosy and that this may result in the introduction of another potent remedy for the treatment of this disease in addition to the present sulphone therapy It is possible that a combination of the two remedies may be more effective than either alone since the mode of action of the two groups appears to be different For leprosy workers the special features of thiosemicarbazone therapy are its probable direct action on the bacillus its beneficial effects on lesions of the mucous membranes and skin its small effective dose (as in case of DDS) and its reported lower toxicity than the sulphones

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ORIGINAL ARTICLES

DIAMINO-DIPHENYL-SULPHONE (DDS) IN THE TREATMENT OF LEPROSY PHARMACOLOGICAL ASPECTS

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INTRODUCTION

Fromm and Wittmann (1908) first prepared diamino-diphenyl sulphone during their researches in dye chemistry This compound did not receive any attention till 1937, when Buttle *et al* (1937), Fourneau *et al* (1937) and Bauer and Rosenthal (1938) found that this substance had great anti-bacterial power against streptococcal infection in mice and to some extent in rabbits and monkeys The interest in the drug was revived when Rist *et al* (1940) showed its favourable effects in experimental tuberculosis in rabbits and guinea-pigs

Though DDS established itself as a powerful anti-bacterial agent in veterinary medicine (Francis, 1947), but because of its toxic effects in doses of the order of 1 to 2 gm a day, it was not used in the treatment of infection in man However, various derivatives have been prepared which are less toxic and could be used with comparative safety

The sulphone derivatives are now well established in the treatment of leprosy, but till recently the parent compound itself was not used on account of its toxicity In recent years, however, successful trials have been carried out with very small doses of this compound given both orally and parenterally by the subcutaneous or the intramuscular route There are two main reasons which led to the trials of DDS in leprosy firstly, the high cost of the proprietary sulphones, and secondly, the evidence to the effect that most of the sulphone derivatives are active by virtue of their breaking down in the body and liberating DDS

Treatment with DDS is no doubt cheap, but great care is needed to standardize the treatment before it can be recommended for use on a large scale In this connection there are two outstanding questions which need solution, and these relate to a suitable dose and the best mode of administration

Regarding the dose it may be said that Cochrane *et al* (1949) used a dose of 2 5 gm a week and found that in this dose the drug produced toxic symptoms which were sometimes alarming, they advocated a dose of not more than 1 5 gm per week Molesworth and Narayanswami (1949) used doses up to 1 gm a week Floch and Destombes (1949) and Muir (personal communication) recommended a dose of 0 2 gm (200 mg) a day,

and Lowe (1950) advocated a daily standard dose of 0.3 gm (300 mg) however of late he (personal communication) is also using 200 mg per day

Regarding the mode of administration it may be said that while Cochrane *et al* and Molesworth and Narayanswami have used the drug parenterally in the form of an oily suspension other workers have used it by mouth In view of the work of Smith (1949) the oral route appears to be quite satisfactory and the parenteral administration seems to have no advantage Smith reported that DDS is quickly and completely absorbed from the gut and is very slowly excreted in the urine so that it is retained for a long time in the body with the result that very small doses (100 to 200 mg a day) are capable of maintaining adequate blood levels of the drug

The objects of the investigations reported herein have been to study the pharmacological aspects of both the parenteral and the oral administration of DDS in order to solve the two outstanding questions regarding its use and thus to determine a suitable dose and method of treatment with it

Material and Methods of Work

The Patients

The study has been made in advanced lepromatous cases of leprosy bacteriologically positive and lepromin negative Sixty-eight patients have been included in the study 31 in patients of the Leprosy Hospital Gobra and 37 patients attending the out patients clinic of the Leprosy Department

The Preparations used in the Study

DDS powder and tablets and a 25 per cent suspension in arachis oil with wax used in the study have all been supplied free by the Imperial Chemical Industries Ltd In case of the oral administration doses from 10 to 50 mg were given in the form of powder accurately weighed and 100 mg as a tablet containing that quantity For the intramuscular route the oily suspension was given by means of a tuberculin syringe

Methods of Work

The investigations have included studies of the following subjects after both oral and intramuscular administration of varying doses and for varying periods

(*i*) Blood concentration and its maintenance

(*ii*) Excretion in urine.

(*iii*) Concentration in skin and other body fluids

(*iv*) Frequent blood examinations for R.B.C. count and hæmoglobin estimation to determine the degree of anæmia produced

(*v*) Frequent van den Bergh test and Schlesinger's test for urobilin in urine to detect hæmolysis and signs of liver damage.

(*vi*) Frequent clinical and bacteriological examination

The Bratton and Marshall method as modified by Brownlee (Brownlee *et al*, 1948) was used for estimating the concentrations of DDS in blood and other body fluids For the estimation of the skin concentrations, a special method was evolved in which the ethyl acetate extract of the skin was used For making the actual readings in all cases, use was made of a photo-electric colorimeter

Blood Concentrations

Earliest Appearance in Blood

Doses from 10 to 100 mg were given both orally and by the intramuscular route The blood was drawn at intervals of 5, 10, 15 and 30 minutes and at 1, 2 and 4 hours after the administration of the drug

All these specimens of blood including the 5 minutes' specimen from both the oral and intramuscular cases showed the presence of DDS, and the concentrations varied from 0 1 to 0 6 mg per cent according to the dose The average blood concentrations after various doses is shown in table I and graph 1 Except for the first 15 minutes the concentrations were higher after oral administration than after intramuscular injections

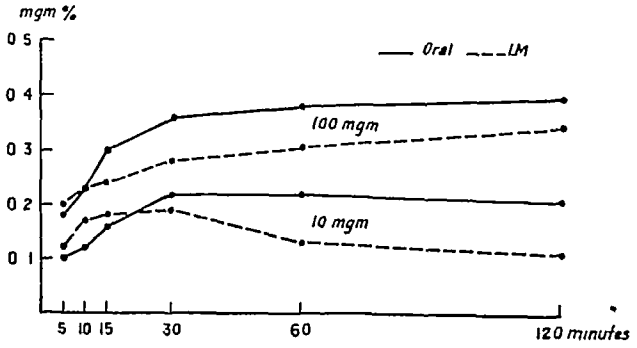
Table I

Blood concentrations of DDS from 5 minutes to 4 hours after administration of first single dose, 10 to 100 mg orally and intramuscularly

Dose in mg	Mode of administration	Number of cases	Average blood concentration of DDS in mg per cent at minutes						
			5	10	15	30	60	120	240
10	Oral	4	0 10	0 12	0 16	0.22	0.22	0.21	0 19
	I M	6	0 12	0 17	0 18	0 19	0 13	0 11	0 08
20	Oral	6	0 13	0 15	0.23	0.26	0.26	0 23	0.23
	I M	5	0 15	0.21	0.20	0.22	0.20	0 16	0 13
50	Oral	8	0 13	0 19	0.21	0.26	0.26	0.29	0.30
	I M	7	0 17	0.20	0.22	0.25	0.22	0.22	0.22
100	Oral	5	0 18	0.23	0.32	0.36	0.38	0 40	0.52
	I M	8	0.20	0.23	0.24	0.28	0.31	0.35	0.38

Graph 1

Average blood concentrations of DDS from 5 minutes to 2 hours after a first single dose of 10 and 100 mg orally and intramuscularly



It can be concluded that appreciable amounts of the drug can be found in the blood as early as 5 minutes after the administration of even a small dose of 10 mg of DDS whether given orally or intramuscularly

With smaller doses (10 and 20 mg) the blood concentration is highest at 30 to 60 minutes and then there is a slight fall the concentration at 4 hours being slightly lower With a bigger dose (50 or 100 mg) the concentration continues to rise and at the end of 4 hours it is slightly higher than at 1 hour (Even after the first single dose the drug can be found in the blood for about 10 days this matter is discussed later)

The Highest Concentration

This question has been studied after (*a*) a single first dose (*b*) repeated administration of the same dose for 8 days and (*c*) prolonged administration of the same dose for about 3 months Doses of 50 100 200 and 300 mg were used for this study but in case of repeated administration the 300 mg dose was discarded after use for a few weeks because of its toxicity (development of rapid anæmia appearance of urobilin in urine positive van den Bergh test and severe lepra reactions)

(*a*) *After the single first dose* —With doses from 50 to 300 mg the highest concentration after oral administration varied from 0 41 to 0.96 mg per cent and after intramuscular administration varied from 0.24 to 0 53 mg per cent By both the routes the maximum concentration is reached 4 to 8 hours after the administration there is then a gradual fall and the concentration at 24 hours is definitely lower than the maximum

concentration The average blood concentration up to 24 hours, after a first single dose, is shown in table II and graph 2

TABLE II

Blood concentrations of DDS up to 24 hours after administration of a first single dose of 50 to 300 mg

Dose in mg	Mode of administration	Number of cases	Average blood concentration in mg per cent at hours						
			1	2	4	6	8	12	24
50	Oral	9	0.28	0.33	0.35	0 41	0.33	0.33	0.23
	I M	5	0 19	0.21	0.24	0.22	0.21	0 19	0.17
100	Oral	8	0.38	0 40	0.52	0.50	0.58	0 43	0.39
	I M	13	0.30	0.35	0.36	0.33	0.28	0.25	0.25
200	Oral	8	0 46	0.54	0 68	0.67	0 66	0 65	0.62
	I M	6	0.32	0.37	0 41	0.34	0 30	0.25	0.25
300	Oral	3	0 65	0.69	0 91	0.96	0 90	0.88	0 70
	I M	4	0.35	0 42	0 45	0.53			0.50

It will be seen that in case of intramuscular administration the maximum concentration after all the doses has been definitely lower than after oral administration (but as shown later the drug is found longer in the blood) It would appear that the drug is absorbed not only more or less completely from the gut, but also more quickly than after intramuscular administration

(*b*) *After repeated administration for 8 days* —The drug was given in various daily doses for 8 days It was then stopped and blood was collected during the next 24 hours The results are shown in table III and graph 2 It will be seen that the blood concentrations in case of both the oral and intramuscular routes are higher than after the first single administration of the same dose, and that the difference in blood concentrations after the two routes begins to disappear

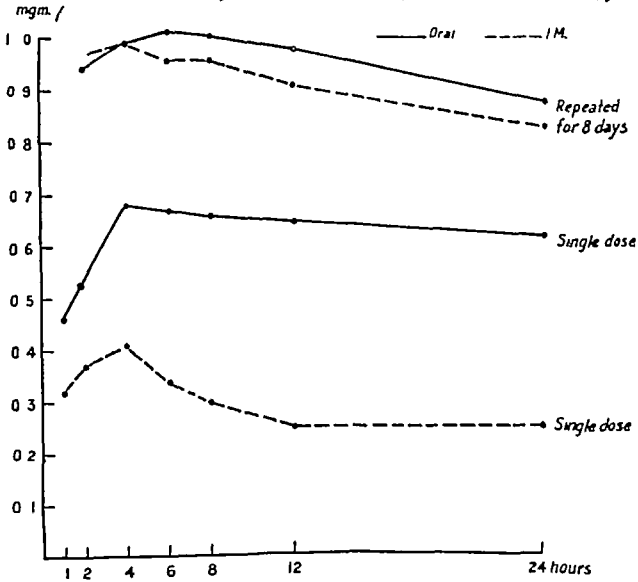
TABLE III

Blood concentrations of DDS up to 24 hours after 8 days' administration of 50 to 300 mg daily

Dose in mg	Mode of administration	Number of cases	Average blood concentration in mg per cent at hours					
			2	4	6	8	12	24
50	Oral	2	0.37	0 47	0 47	0 47	0 45	0.25
	I M	4	0.31	0 42	0 41	0.36	0.29	0.27
100	Oral	4	0 76	0.83	0 95	0 92	0 77	0 60
	I M	5	0 60	0 64	0 64	0 60	0.58	0.57
200	Oral	4	0 94	0.99	1 10	1 00	0 98	0.88
	I M	5	0 96	0 99	0 96	0.96	0 91	0.83
300	Oral	4	1 00	1 40	1.57	1 65	1 64	1 10
	I M	2	1 05	1.35	1 45	1.55	1 65	1 10

Graph 2

Average blood concentrations of DDS after (i) a single dose of 200 mg and (ii) the same dose repeated daily for 8 days, orally and intramuscularly



(c) *After prolonged administration* —The drug in various daily doses was given for about 3 months It was then stopped, and the blood concentrations during the next 24 hours were estimated

TABLE IV

Blood concentrations of DDS after doses of 50 100 *and* 200 *mg given* (i) *as a single dose* (ii) *for* 8 *successive days and* (iii) *continuously for* 3 *months*

Dose in mg.	Mode of administration	After a single dose				After 8 days daily				After prolonged administration daily			
		4	8	12	24	4	8	12	24	4	8	12	24
50	Oral	0.33	0.33	0.33	0.23	0.47	0.47	0.45	0.25	0.52	0.50	0.47	0.36
	I.M.	0.21	0.21	0.19	0.17	0.42	0.36	0.29	0.27	0.50	0.16	0.39	0.36
100	Oral	0.52	0.58	0.43	0.39	0.83	0.92	0.77	0.60	0.88	0.84	0.69	0.60
	I.M.	0.36	0.28	0.25	0.25	0.64	0.60	0.58	0.57	0.70	0.70	0.07	0.58
200	Oral	0.67	0.80	0.87	0.65	0.99	1.00	0.99	0.88	1.10	1.10	0.99	0.81
	I.M.	0.41	0.30	0.25	0.25	0.99	0.90	0.91	0.83	0.95	0.93	0.91	0.84

The findings made after prolonged administration of 50, 100 and 200 mg daily doses are shown in table IV, which also includes comparative figures after a single dose, and after administration for 8 days It will be seen that the concentrations after prolonged administration were only slightly higher than those after 8 days administration, and that the difference between the concentrations after the two routes had practically disappeared The highest concentration with a 50 mg daily dose was about 0 5 mg per cent and with 100 to 200 mg daily dose about 1 mg per cent (with 300 mg daily it was 2 mg per cent, not shown in the table)

The blood concentrations reported above are generally in agreement with the results reported by some other workers, although no report is as exhaustive as the present one Smith (1949) has reported that on oral doses of 100 to 400 mg a day, the mean minimal blood concentration varies from 0 4 to 1 5 mg per cent according to the doses, it being 1 mg on a dose of 300 mg Cochrane *et al* (1949) found the blood concentrations ranging between 0 7 to 2 mg per cent and they suggested that it should not be allowed to rise above 2 mg per cent Lowe (1950) has reported that on a daily dose of 100 to 500 mg the blood level varies from 0 5 to 2.2 mg per cent according to the doses, it being 0 8 to 1 4 mg per cent on a dose of 300 mg

How long the Drug is found in the Blood

This question has also been studied after (*a*) a single first dose, (*b*) repeated administration of the same dose for 8 days, and (*c*) prolonged administration of the same dose for about 3 months Doses of 100 and 200 mg were used for this study and observations were made in 30 patients

The results with the 100 and 200 mg doses were similar and are summarized in table V and graph 3 The information summarized in table V brings out the following points

(*i*) Even after a single dose of 100 to 200 mg traces of the drug in the blood can be found for about 8 to 12 days

(*ii*) After repeated administration, the period for which the drug can be found in the blood after stopping the treatment, is much longer, up to 35 days

(*iii*) That this period is appreciably longer after intramuscular administration than after the oral route

TABLE V

Average period for which DDS can be found in the blood after cessation of treatment with 100 and 200 mg daily

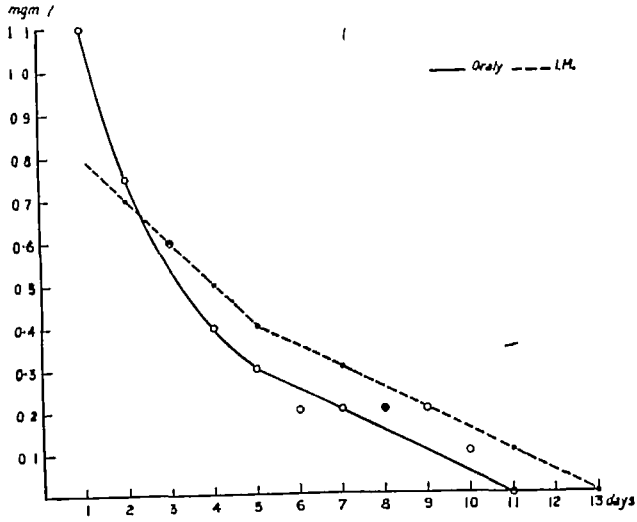
Duration of treatment	NUMBER OF DAYS TILL THE END OF WHICH A BLOOD CONCENTRATION OF 01 MG PER CENT WAS FOUND	
	Intramuscular	Oral
One day	8 to 12	6 to 10
Daily, for 8 days	10 to 13	6 to 11
Daily, for 2 to 3 months	19 to 35	12 to 15

Smith (1949) found that DDS was still detectable in blood 14 days after cessation of a 6 weeks period of administration by mouth

Graph 3 shows the average blood concentrations during rest period following the administration of 200 mg DDS orally and intramuscularly for 8 days It will be seen that for the first two days after stopping the treatment (as also during the course of treatment) the blood concentrations

Graph 3

Main enance of blood concentration of DDS during rest period after administration for 8 days of 200 mg daily orally and intramuscularly



are higher in case of the oral administration However the fall in blood concentration is more rapid in this case than in the case of intramuscular administration with the result that from the 3rd day onwards after stopping the treatment the concentrations become lower and the blood becomes free of the drug earlier than in case of the intramuscular route

Blood Concentrations with the Drug given less frequently

So far the findings made with daily administration of the drug have been discussed Since the drug is eliminated very slowly a study was made of the resulting concentrations from administration of the drug on alternate days and twice a week to find out whether the interval could be

increased without seriously affecting the blood concentration The comparative findings are shown in table VI and graphs 4 and 5

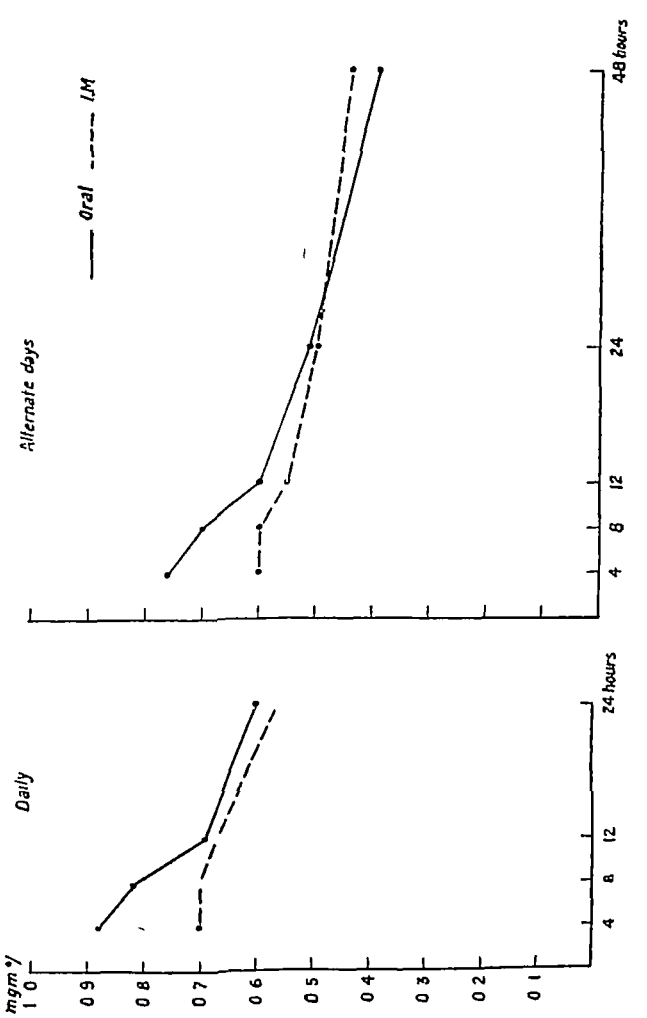
It will be seen that in case of treatment on alternate days blood concentrations are at all times lower than on daily administration of the

TABLE VI

Blood concentrations of DDS on same dose given at varying intervals

Dose in mg	Mode of administration	Daily mg per cent at hours				Alternate days mg per cent at hours					Bi-weekly mg per cent at hours							
		4	8	12	24	4	8	12	24	48	4	8	12	24	48	72	96	
100	Oral	0.88	0.84	0 69	0 60	0 77	0 70	0.60	0.51	0 40								
	I M	0 70	0 70	0.67	0.56	0 60	0 60	0.55	0.51	0 44								
200	Oral	1.10	1.10	0.99	0.81	0.88	0 76	0 71	0.58	0 45	0 70	0 60	0 49	0 43	0.26	0.23	0 12	
	I M	0.95	0.95	0.91	0.84	0.65	0.62	0.58	0.53	0 47	0.54	0 43	0 43	0.39	0.36	0.31	0.20	
300	Oral	1.60	1.80	1 75	1.30						1.05	1.10	1 00	0 73	0.59	0 42	0.24	
	I M										0.66	0 70	0 63	0 61	0.57	0.53	0.37	

same dose This is specially marked in the second 24 hours, and particularly with the oral route



Graph 4.
Average blood concentrations of DDS after administration of 100 mg DDS by mouth and intramuscularly daily and on alternate days.

TABLE VII

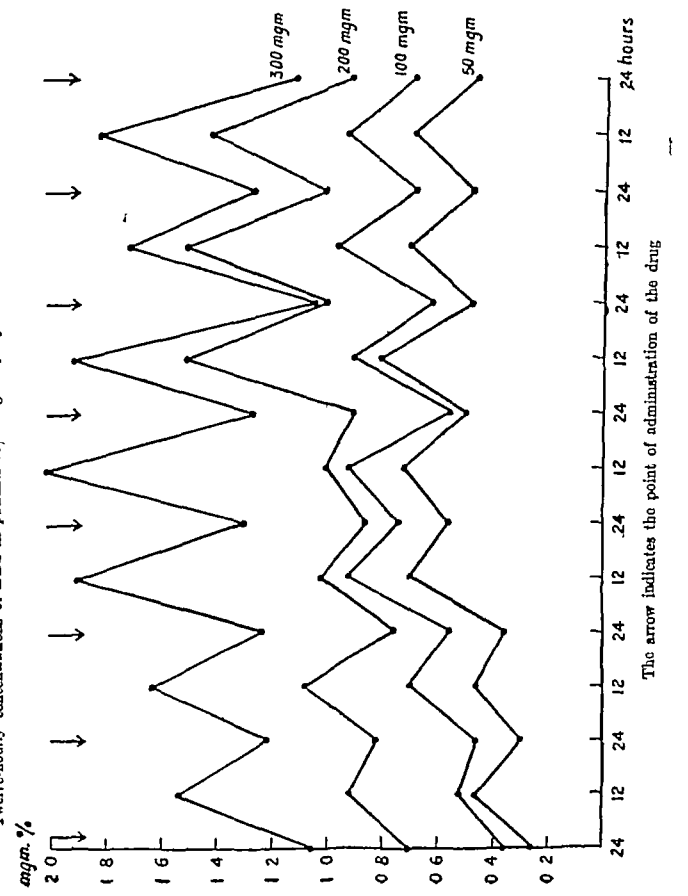
Twelve and twenty-four hours' blood concentrations in cases treated daily with DDS by oral and intramuscular administration

Dose in mg	Mode of administration	Number of cases	Blood concentration of DDS in mg per cent													
			1		2		3		4		5		6		7 days	
			12	24	12	24	12	24	12	24	12	24	12	24	12	24 hours
50	Oral	2	0 45	0.30	0 45	0.37	0 70	0.57	0 72	0.50	0.80	0 47	0 70	0 47	0 67	0 47
	I M	2	0.35	0.35	0.57	0.57	0 60	0.57	0.62	0.57	0.65	0 60	0 67	0.55	0.67	0.50
100	Oral	2	0.50	0 45	0 70	0.57	1 00	0 75	0.92	0.55	0.87	0 60	0.95	0.67	0 92	0.67
	I M	2	0 71	0.55	0.68	0 65	0 66	0 65	0 70	0 65	0 70	0 60	0 75	0 65	0 75	0.60
200	Oral	2	0.92	0.82	1 00	0 77	0 95	0.87	1 00	0 90	1.50	1 00	1.50	1 00	1 40	0.90
	I M	2	1 10	0 62	1.20	0 70	1.20	0.97	1.25	1 10	1.37	0 97	1 00	0 77	1 10	0 77
300	Oral	2	1.57	1.22	1 62	1.27	1.90	1.30	2 00	1.27	1.80	1 00	1 70	1.27	1.80	1 10
	I M															

have already been considered The findings made during the studies have shown that

(i) Absorption from the two routes is about equally complete and rapid

(ii) The elimination is very slow after either route and the drug is retained for long after the last dose the period being a little longer in case of intramuscular administration



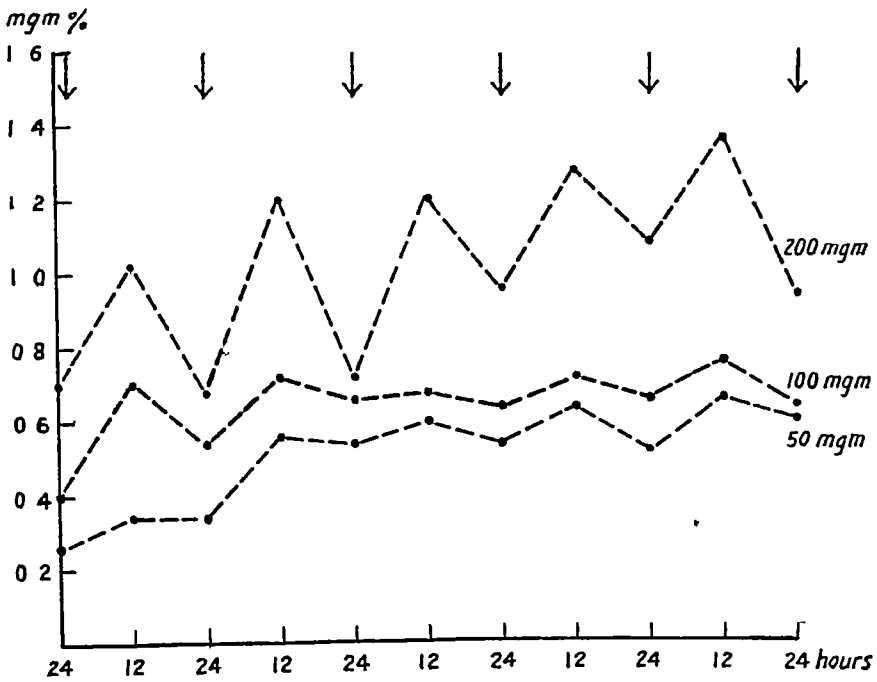
Graph 6.

Twelve-hourly concentrations of DDS in patients receiving daily by mouth 50 100 200 and 300 mg

(*iii*) Concentration reached after a certain dose is slightly higher after the oral administration

Graph 7

Twelve-hourly concentration of DDS in patients receiving daily intramuscular injections of 50, 100 and 200 mg



The arrow indicates the point of administration of the drug

From the above observations it can be concluded that intramuscular route has no advantage over the oral route This is true not only for daily administration by either route, but also in case of bi-weekly injections as compared to the daily oral administration

The question for special consideration is that whether intramuscular administration has any advantage for the patients in whom daily treatment is not feasible, and treatment has to be given bi-weekly A reference to table VI and graph 5 would show that even for bi-weekly treatment intramuscular route offers no advantage over the oral route It will be seen that for the first two days after a bi-weekly dose the concentration is higher in case of oral administration, while for the next two days it is slightly higher in case of the intramuscular administration It would therefore appear that, if for any reason daily treatment cannot be given, oral administration of a bi-weekly dose is as good as an intramuscular injection at that interval Lowe (personal communication) is using this method (oral bi-weekly) in Nigeria

While the intramuscular administration offers no advantage, it has a definite disadvantage since after repeated injections there is good deal of induration at the sites of injections, and not infrequently these lead to abscess formation which may have to be opened up The material obtained

from such abscess shows a high concentration of DDS (up to 40 mg per cent)

TABLE VIII

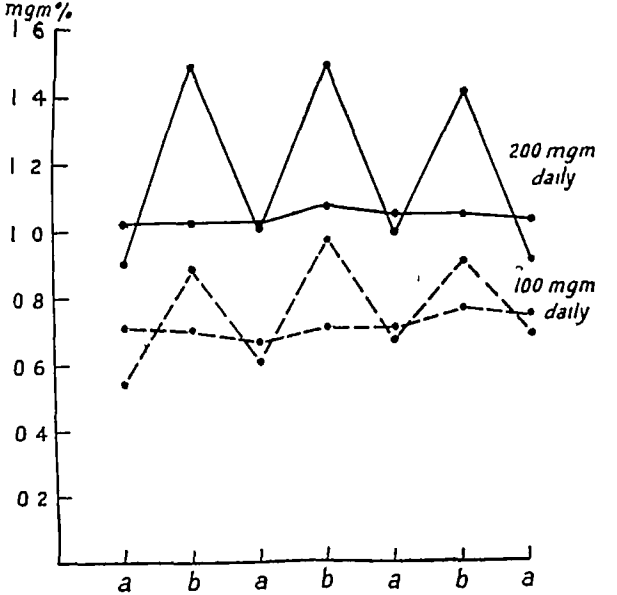
Twelve hourly blood concentrations of DDS following oral administration of 100 and 200 mg given as (i) a single dose and (ii) two divided doses at 12 hours' interval

Total daily dose in mg	How given	Number of cases	Average blood concentration in mg. per cent at hours						
			a	b	a	b	a	b	a
100	2 divided doses	2	0.70	0.70	0.67	0.70	0.70	0.77	0.70
100	Single dose	2	0.55	0.87	0.60	0.95	0.67	0.92	0.6
200	2 divided doses.	2	1.01	1.01	1.01	1.02	1.02	1.02	1.01
200	Single dose	2	0.90	1.50	1.00	1.50	1.00	1.40	0.90

a = 24 hours in case of single administration and 12 hours in case of twice daily administration
b = 12 hours after administration

Graph 8.

Blood concentration of DDS following oral administration of 100 and 200 mg given as *(i) a single dose and (ii) two divided doses at 12-hour intervals*



a 24 hours after the single dose and 12 hours after the divided dose.
b 13 hours after the dose

Excretion of DDS in Urine

This matter has been studied from the point of view of (*a*) earliest appearance in the urine, (*b*) highest concentration, (*c*) longest period for which it is found in the urine, (*d*) total excretion, and (*e*) relationship between blood and urinary concentrations

(*a*) *Earliest appearance in the Urine*

This question has been studied only in case of a first single dose since in patients under treatment the drug will be found in the urine at all hours

Doses of 10, 20, 30, 40, 50 and 100 mg were used for the purpose, and it was found that with all these doses, DDS appears in the urine 20 to 30 minutes after its oral or parenteral administration The initial urinary concentration is about 1 mg per cent, and with doses of 50 to 100 mg it gradually rises to about 5 mg per cent, reaching that level in about 4 hours

(*b*) *Highest concentration in the Urine*

This matter was studied in cases receiving daily treatment with DDS The concentration after the same dose was found to be higher in case of oral administration than after the parenteral administration The results with 100 mg daily doses are shown in table IX

Table IX

Maintenance of urinary concentration on stopping the treatment after 100 *mg daily given for varying periods*

Length of treatment	Mode of administration	Highest concentration in mg per cent	Day till which 1 mg per cent found
1 day	Oral	7	6
	I M	3	10
8 days	Oral	15	8
	I M	12	12
2 months	Oral	16	25
	I.M	14	35

It may be stated that with a dose of 50 mg daily the highest average concentration was 5 mg per cent, with a dose of 100 mg it was 5 to 10 mg per cent and with a dose of 200 mg it was 10 to 15 mg per cent There may, however, be marked individual variations

(*c*) *How long the Drug is found in Urine*

DDS can be found in urine for a considerable period after stopping the treatment with it Naturally this period varies with the dose and the length of treatment The findings made with a daily dose of 100 mg are shown in table IX The following observations can be based on these findings

(1) Following a single dose of 100 mg DDS is found in the urine till 6 to 10 days after administration

(ii) Following treatment for 8 days it can be found for 8 to 12 days and following 2 months treatment for 25 to 35 days after stopping the treatment

(iii) With the same dose used for the same length of time, the drug is excreted for a longer period after the intramuscular route, although urinary concentrations are higher after the oral route.

With doses bigger than 100 mg the concentrations were higher and the period for which the drug could be found in the urine was longer

(*d*) *Total excretion in Urine*

This matter was studied in patients who had been under treatment for about 3 months to allow sufficient time for the conditions to become stable. Preliminary investigations showed that the urinary concentration on different days were not constant Twenty four hour collections of urine were therefore made on 3 successive days and total excretion of DDS in these specimens was estimated and a mean of these figures was worked out These means are shown in table X

TABLE X

Average daily excretion of DDS in urine in patients who had been under treatment for about 3 months

Daily dose in mg.	Mode of administration	URINARY EXCRETION	
		Average total daily excretion in mg	Percentage of daily intake
50	Oral	35	70
	I.M	36	72
100	Oral	75	75
	I M	65	65
200	Oral	126	63
	I.M	120	60

It will be seen that 60 to 75 per cent of the daily DDS intake can be accounted for in the urine A fact which is not shown in the table is that

the daily excretion is not constant and that considerable variations are seen from day to day

It may be stated that our figures regarding the total urinary excretion are similar to those of Smith *et al* (1949) who recovered 70 per cent of the drug (DDS) from urine of rabbits fed on it Smith (1949) working with leprosy patients treated orally with DDS found that on an average 83 per cent of the daily intake was excreted in urine

(*e*) *Relationship between Blood and Urinary concentrations*

The relevant data on this point have already been considered The relationship between blood and urinary concentrations may be summarized as under

(*i*) The drug appears a little earlier in blood than in urine

(*ii*) Urinary concentrations are always higher (5 to 10 times) than blood concentrations

(*iii*) After cessation of treatment the drug can be found longer in urine than in blood

(*iv*) The above relationship holds good for both the oral and the intramuscular routes

DDS Concentration in Skin

During studies with sulphetrone (Dharmendra, Dey, Bose and Kapur, 1950) it was found that skin and blood concentrations are similar irrespective of the dose, mode of administration and the interval since the last dose Similar findings have been made with respect to DDS

With the routine Bratton and Marshall method for the estimation of sulphones, normal skin gives rise to a slight colour reaction which in case of sulphetrone was found to be equal to about 0 3 mg per cent, and this had to be allowed for while making final calculations of skin concentrations of the drug However, this method is not very satisfactory, since the depth of the colour produced by normal skin is not constant, but varies with the amount of skin used for the test, and to some extent with individual skins In case of DDS a better method has been evolved which altogether eliminates this factor The skin is extracted with ethyl acetate and this extract is used for making the estimation

One worker has recently suggested that the concentration of sulphones is much higher in real skin (epidermis and dermis), and that the drug is absent from the subcutaneous tissue removed with skin biopsy He has tried to explain the fact of not finding a high skin concentration as caused by the inclusion of a large amount of subcutaneous tissue in the skin specimen used for the estimation This matter has also been investigated and this view has not been confirmed

The results of investigations on skin concentration are shown in table XI From this table it will be seen that

(i) Blood and skin concentrations are similar in all cases

(ii) Except in one case concentrations in the whole skin epidermis and subcutaneous tissue have been similar

(iii) The similarity between skin and blood concentration is found irrespective of the blood level dose mode of administration and the interval since the last dose

TABLE XI

Comparative blood concentrations of DDS in blood sweat and skin (whole skin epidermis—dermis and subcutaneous tissue)

Name	Length of treatment in weeks	Total dose in gms.	Mode of administration	Present dose	Concentration of DDS in mg. per cent				
					Skin*			Sweat	Blood
					Whole skin	Epidermis and dermis	Subcutaneous tissue		
J D	14	8	I.M	200 mg alternate days	0·43	0·55	0·45		0·45
M J	14	8	"	"	0·45	0·86	0·36		0·50
J M	23	11		200 mg bi weekly	0·43	0·50	0·50		0·50
S B	23	9	"		0·45	0·40	0·47		0·45
B S	16	7		"	0·50				0·50
S S	26	16	Oral	200 mg alternate days	0·69			2·0	0·70
B R	27	16			1·00	0·98	1·01	0·7	0·95
S D	22	8		100 mg daily	0·54	0·55	0·55	1·0	0·55
D S	21	18		"	0·75	0·75	0·75	0·5	0·70
S. C	25	13	"	"	0·66			0·8	0·60
B C	24	14	"		0·78	0·78	0·78	0·4	0·70
S K.	28	21	"	"	0·83	0·84	0·80	0·7	0·85
K B	31	14	"		0·78	0·78	0·78	0·8	0·75
P D	26	30		Rest period	Nil†				Nil†
A. H.	26	31		"	Nil†				Nil†

* Ethyl acetate extract method

† In these cases DDS was absent from urine also they had been off treatment for over 4 weeks.

DDS concentration in Sweat, Saliva and Tears

DDS concentration in sweat was estimated in 20 patients and concentrations in saliva and tears in 15 of these patients The findings in individual cases are shown in table XII and the average figures are given

Table XII

DDS concentrations in sweat, saliva and tears (The concentrations in blood and urine are included for comparison)

Name	Total dose in gm	DDS concentration in mg per cent				
		Blood	Urine	Sweat	Saliva	Tears
S C	13	0 60	12.50	0.80		
S S	16	0 70	8.50	2 00		
S D	8	0.55	4 00	1 00		
D S	18	0 70	2.50	0.50		
B R	16	0 95	2.50	0 70		
B C	14	0 70	4.50	0 40	0.50	0 70
S K	21	0.85	5 00	0 70	0.50	0.50
B B	25	1 40	10 00	1 10	0 60	0 40
R M	14	0.50	4.50		0.30	0.30
K B	14	0 75	8.00	0.80	1 00	0.80
M G	15	0 40	2 00	0 45	0.30	0.30
S D	8	0.85	6.50	0.90	0.50	0.60
A D	14	0 75	10 00	0 40	0.25	0.60
S D	15	0.80	9.50	0 95	0.60	0 75
G J	8	0.85	12 50	1 00	0.50	0.90
P S	26	1.15	2.50	1 05	0 75	0 75
S R	15	0 90	0 70	0.50	0 60	0.38
R R	8	0 75	2.50	0 65	0 45	0.56
M H	8	1 00	9 00	0 90	0.55	0 40
A M	8	0 60	2.50	0 62	0 45	0.30

All the above patients were on oral treatment, and the dose was 100 mg daily except in two, who were on 200 mg daily

in table XIII In these tables are also included blood and urinary concentrations in the same patients at the same hour All these patients were on oral treatment with 100 mg daily, except two who were receiving 200 mg daily

Table XIII

Average DDS concentrations in various body fluids and skin in patients treated with daily doses of 100 mg of the drug

Tissue	DDS concentration in mg per cent
Blood	0.8
Sweat	0 7
Skin	0 7
Tears	0.6
Saliva	0.5
Urine	6 0

The concentration in the sweat varies to some extent according to the quantity secreted but on the whole it is similar to the blood and skin concentrations The concentration in saliva and tears is of the same order as the blood concentration (urinary concentration is however much higher)

Toxicity and Complications

The Tests used

For assessing toxicity the following examinations were frequently done Total R B C count Hæmoglobin estimation, van den Bergh test, and Schlesinger s test for urobilin In addition the clinical findings in the patients provided useful information in this respect

Anæmia

In common with other sulphone drugs, DDS gives rise to a fall in R B C and Hæmoglobin Moreover as judged by the results of the van den Bergh and Schlesinger s tests it appears that DDS even in small doses is comparatively more hæmolytic than its derivatives in common use. The findings are analysed in table XIV which describes the effect of varying doses of DDS on total R B C Hæmoglobin plasma bilirubin urobilin and production of reaction or exacerbation of the disease

The fall in R B C and Hæmoglobin is proportionate to the dose After a dose of 50 mg daily there is only a slight fall on an average less than half a million R B C and ½ gm Hæmoglobin after a dose of 100 mg daily a fall of about one million R B C and 2 gm Hæmoglobin and after a dose of 200 mg daily a fall of little more than 1 million R B C and 3 gm Hæmoglobin In most cases but not in all the blood picture improved after an initial fall The anæmia produced by a daily dose of 300 mg has not been studied in detail since this dose was tried only in a small number of cases and was not continued for more than 3 weeks as during this period it gave rise to a considerable anæmia and high incidence of positive van den Bergh and Schlesinger's tests and severe lepra reaction in three of the five cases and one of these three developed jaundice

Results of the van den Bergh and Schlesinger s Tests

These tests have always been negative with doses of 50 mg daily and twice daily but in higher doses they have been occasionally positive With 100 mg daily positive findings were made at some time during treatment in about one-quarter of the cases and with 200 mg daily in about half the cases Observations on 300 mg doses were not extended as this dose was not considered safe

Regarding the results of these tests it may be said that positive findings have no doubt been made much more frequently with DDS than with sulphetrone however these positive findings have only been occasional and not persistent Moreover the degree of positivity has been low in case of the van den Bergh test positive results have been seen only by the indirect method and the quantitative test has shown the presence of plasma bilirubin only up to 1 mg per cent except in a few cases in case of the Schlesinger's test positive result was seen mostly with undiluted specimens of urine and a 1 in 10 dilution usually gave negative result Moreover positive findings with these tests were more frequently made during the early part of treatment than later it may be mentioned that the fall in

TABLE XIV

Effects of varying doses of DDS on total R B C, hæmoglobin, plasma bilirubin, urobilin and production of reaction, etc

Dose in mg	Number of cases	Average duration of treatment in weeks	Average total dose in gms	Range of blood concentration	Average fall of R.B.C in million	Average fall of Hb in gms	Number showing positive		Average period of suspension of treatment in weeks†	Number of cases suffering from reaction
							Van den Bergh* (indirect)	Urobilin* (undiluted)		
50 (single)	12	11	6	0.5–0.7	0.2	0.5	0	0	Nil	Nil
50 (b.d)	9	8	7	0.7–0.8	0.6	1.0	1	0	Nil	Nil
100 (single)	36	11	8	0.7–1.0	0.8	1.9	9	6	2	11 (30%)
100 (b.d)	13	9	15	1.0–1.1	0.8	1.8	4	4	2.3	3 (23%)
200 (single)	16	13	18	0.9–1.4	1.0	3.0	8	8	3.5	8 (50%)
300 (single)	5	3	5	1.1–2.4	1.3	3.8	4	4	3	3 (60%)

*In the cases showing positive results, the positive findings were made only occasionally and were within the high normal range

†Treatment had to be suspended in several cases due to either a reaction, marked anæmia, or abscess formation after intramuscular administration

R.B.C. and Hæmoglobin is also seen more frequently in the early parts of the treatment. Thus the findings with both the tests in most cases fall within the high normal range of bilirubin and urobilin and as such do not indicate the development of any serious situation. But they do indicate that DDS is more likely to produce hæmolysis than its derivatives.

Febrile and Eye Reactions

With a dose of 50 mg. daily or twice daily, no such reactions were seen but they were frequent on 100 to 300 mg. daily doses the incidence rising with the dose.

Apart from these reactions a large number of patients got crops of short lived painful nodules of the nature of erythema nodosum. With DDS this was seen more frequently than in patients treated with its derivatives.

Other Symptoms

A very common complaint was a burning sensation in hands and feet specially at the beginning of the treatment. this was usually relieved by yeast or Vitamin B complex. Several patients complained of weakness specially in the early part of treatment. In a few patients signs of mental depression were evident.

A complication not infrequently seen after repeated intramuscular administration of the oily suspension was the development of a localized abscess at the site of injection. The contents of the abscess obtained by aspiration or when the abscess burst open showed very high concentrations of DDS (up to 40 mg. per cent).

In patients receiving 100 to 300 mg. daily treatment had often to be suspended, on account of a severe reaction, marked anæmia or development of a painful abscess following intramuscular administration. This contingency did not arise in the cases receiving 50 mg. daily or twice daily.

CONCLUSIONS REGARDING DOSE AND MODE OF ADMINISTRATION

As indicated in the introduction the main object of the investigations reported herein was to find out a suitable dose and mode of administration for DDS. The findings made during the study have already been considered and the following conclusions can be based on these findings.

Mode of administration

(1) For DDS the oral administration is the method of choice, since in case of this drug the intramuscular route offers no advantage. This applies not only to daily but also to bi weekly treatment. If for any reason treatment cannot be given daily oral administration twice a week is as good as an intramuscular injection at that interval.

(2) For oral administration it is better to give the total daily quantity in two divided doses than as a single daily dose. The divided doses produce a more constant blood concentration throughout the 24 hours and the toxic effects are less marked.

Dose

(1) The maximum daily dose should not exceed 200 mg, as higher doses are not considered safe When this quantity is given as a single daily dose the average daily range of blood concentration of DDS is between 1 0 and 1 5 mg per cent However, when this is given in the form of two divided doses of 100 mg each a more or less constant blood concentration of 1 0 mg per cent is maintained throughout the 24 hours

(2) Treatment should be started with 50 mg daily and the dose gradually increased to 50 mg twice daily, and worked up to 100 mg twice daily in about 4 weeks Treatment should be given for 6 days a week and occasionally there should be longer periods of rest for 1 or 2 weeks

(3) A matter for special consideration is whether a dose of 100 mg a day will not meet the requirements If this dose is found equally or only slightly less effective, it would certainly be preferable This matter needs further consideration and is being looked into It may be stated that a dose of 50 mg twice daily (100 mg a day) would maintain a more or less constant blood concentration of about 0 7 mg per cent throughout the 24 hours

SUMMARY

1 Diamino-diphenyl-sulphone (the ~~present~~ Parent compound of the sulphone drugs) is very toxic in doses of the order of 1 to 2 gm daily, but has recently been used in small doses in the treatment of leprosy However, the questions regarding the most suitable dose and the best method of administration have still to be answered The investigations reported in this paper were undertaken to provide a solution to these two outstanding questions

2 The study has been carried out in 68 advanced lepromatous cases bacteriologically positive and lepromin negative The investigations have included the absorption, resulting blood concentration and its maintenance, excretion in urine, drug concentration in skin and body fluids, and tests for anæmia and liver damage after both oral and intramuscular administration of varying doses for varying periods

3 Regarding the absorption of the drug, the resulting blood concentrations and their maintenance, the following conclusions can be drawn

(*i*) The drug is quickly absorbed from the gut as after the intramuscular injection, appreciable amount of it could be found in blood as soon as 5 minutes after the administration of even a small dose of 10 mg by either route

(*ii*) The highest blood concentration of the drug is reached 4 to 8 hours after administration by either route After treatment for about a week, the highest blood concentration is about 0 5 mg per cent on a dose of 50 mg a day, a little below 1 0 mg per cent on a dose of 100 mg a day, a little above 1 mg per cent on a dose of 200 mg a day, and about 1 5 mg per cent on a dose of 300 mg a day The concentrations after intramuscular administration were slightly lower than after oral administration of the same dose

(iii) When the treatment is given less frequently (on alternate days or twice in week) blood concentrations at all hours are considerably lower than after daily administration of the same dose This applies to both the oral and the intramuscular routes

(iv) The range of blood concentration in patients on a single daily dose was investigated by examining two daily samples of blood one 12 hours and the other 24 hours after the dose The average range with the oral route for a dose of 50 mg daily is between 0 7 and 0 5 mg per cent, for 100 mg daily between 0 9 and 0.7 mg per cent and for a 200 mg daily between 1 4 and 1 0 mg per cent With the intra muscular route however the 12 hourly variations are less marked

(v) It is possible to eliminate the variations seen in the blood concentration on a single daily dose by dividing it into two equal doses given twice daily With a dose of 50 mg twice daily (100 mg a day) the blood concentration of DDS at 12 and 24 hours is about 0 7 mg per cent and with a dose of 100 mg twice daily (200 mg a day) it is about 1 mg per cent

(vi) The drug is excreted slowly mainly through the kidneys and it can be found in blood (and urine) long after cessation of treatment with it This period varies according to the dose and length of treatment For a dose of 100 to 200 mg it may be said that (a) even after a single dose traces of the drug in the blood can be found for about 8 to 12 days and (b) after repeated administration this period is much longer up to 35 days This period is slightly longer after intra muscular than after oral administration

(vii) As judged by the resulting blood concentrations and their maintenance after oral and intramuscular administration of varying doses and at varying intervals it can be concluded that in the case of this drug the intramuscular route has no advantage over the oral route This applies not only to daily but also to bi weekly treatment

4 Regarding the excretion of the drug in the urine the following conclusions can be drawn —

(i) The drug appears in urine 20 to 30 minutes after oral or parenteral administration of even a small dose of 10 mg

(ii) The highest urinary concentration is on an average about 5 mg per cent with a dose of 50 mg daily up to 10 mg per cent with a dose of 100 mg daily and up to 15 mg per cent with a dose of 200 mg daily As in the case of blood concentration the urinary concentration with the same dose is a little higher after the oral than after the intra muscular route

(iii) The drug is found in the urine for long after the cessation of treatment with it as in the case of blood this period is a little longer after the intramuscular than after the oral route

With a dose of 100 mg daily continued for two months, DDS can be found in urine for 25 to 35 days after stopping the treatment, with higher doses this period is longer

(*iv*) When the treatment has been continued for some time, 60 to 75 per cent of the daily DDS intake can be accounted for in the urine

(*v*) Urinary concentrations are always higher than blood concentrations, and after cessation of treatment drug can be found longer in urine than in blood This relationship between the blood and urinary concentrations holds good for both the oral and the intramuscular routes

5 No evidence has been found of the concentration of the drug by the skin, the concentrations in blood, skin, sweat, saliva and tears have been of the same order The similarity between skin and blood concentrations is found irrespective of the blood level, dose, mode of administration and the interval since the last dose

6 In common with the other sulphone drugs, DDS gives rise to a fall in R B C and Hæmoglobin Moreover, as judged by the results of the van den Bergh and the Schlesinger's tests, even in small daily doses of 100 to 300 mg, DDS appears to be more hæmolytic than its derivatives in common use

7 With a dose of 50 mg daily or twice daily, no febrile or eye reactions were seen, but they were frequent on 100 to 300 mg doses, the incidence rising with the dose The dose of 300 mg a day was discarded after a short trial because of its toxicity

8 Other toxic symptoms include a feeling of weakness and a burning sensation in hands and feet, specially in the early part of treatment In a few patients signs of mental depression were evident

9 Regarding the dose and mode of administration of DDS the following conclusions can be based on the above observations

(*i*) The oral administration is the method of choice, since in case of this drug the intramuscular route offers no advantage If for any reason treatment cannot be given daily, the oral administration twice a week is as good as an intramuscular injection at that interval

(*ii*) For oral administration it is better to give the total daily quantity in two divided doses than as a single dose The divided doses produce a more constant blood concentration throughout the 24 hours and the toxic effects are less marked

(*iii*) The maximum daily dose should not exceed 200 mg

(*iv*) Treatment should be started with 50 mg daily and the dose gradually increased to 50 mg twice daily, and worked up to 100 mg twice daily in about 4 weeks

(*v*) If a dose of 100 mg daily is found equally or only slightly less effective it would certainly be preferable This matter is being investigated

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REPRINTED ARTICLE

TREATMENT OF LEPROSY WITH DIAMINO-DIPHENYL SULPHONE BY MOUTH

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Diamino-diphenyl sulphone (D.A.D.P.S.) was the first sulphone synthesized (Fromm and Wittman, 1908), but its pharmacology and therapeutic effects were not studied until 1937, when Buttle *et al* found that it possessed remarkable properties. In streptococcal infections in mice, doses of 0·4 mg. were as effective as doses of sulphanilamide a hundred times greater, and doses of 0·04 mg. were only slightly less effective than 0·4 mg. In protection tests, 2 mg. gave better results than 50 mg. of sulphanilamide. Its acute toxicity was however ten to twenty times greater than that of sulphanilamide.

Also in mice, Bauer and Rosenthal (1938) reported similar findings. Buttle *et al* (1937) also studied the effects of D.A.D.P.S. in rabbits and in monkeys. In rabbits, the results were less striking than in mice, but still very good. In monkeys, the antibacterial activity of the blood after a dose of 1 g. of D.A.D.P.S. was about the same as after 4 g. of sulphanilamide, and the effect was more lasting. Further work in other animals followed, and D.A.D.P.S. later became established as a powerful antibacterial agent in veterinary medicine (McEwen *et al*, 1941; Francis, 1947).

In man Buttle *et al* (1937) found that after a single dose of 300 mg. the blood had definite antibacterial properties, but no detailed studies were reported. Subsequently (Buttle, personal communication), a therapeutic trial was made in human beings with acute infections, doses of the order of 1 to 2 g. a day were given but because of the rapid production of methæmoglobinæmia and other toxic effects the treatment was soon abandoned. The only other information available to me on the toxicity of D.A.D.P.S. in man is a statement made by Long and Bliss in 1939 and quoted by Feldman *et al* (1944) that D.A.D.P.S. was considered too toxic for use in man.

There seem to have been no attempts to determine the therapeutic blood-level needed in man or the dosage necessary to produce that level. The little work that was done in man was with doses fixed arbitrarily at a level now believed to have been far too high.

When Rist *et al* (1940) demonstrated the action of sulphones in experimental tuberculosis in animals, D.A.D.P.S., 'promin' and 'diasone' were used in the extensive animal experiments which followed. D.A.D.P.S. showed up well, producing some results comparable to those of other sulphones in higher doses. In this work Feldman and his collaborators were prominent. Feldman (1946), in summarizing the work, made no statement regarding the relative efficacy of the different sulphones. It is worthy of

note that Smith *et al* (1942) found that *in vitro* D.A.D.P.S. was ten times as active as promin.

In the trials of sulphones in human tuberculosis because of its reputed toxicity to man no attempt seems to have been made to use D.A.D.P.S. possibly the most potent sulphone. The results of sulphone treatment in human tuberculosis have been disappointing.

The Sulphones in Leprosy

This work started in the United States in 1941 and continued since, has been well summarized by Faget (1947) and by Sharp and Payne (1948). Workers in the United States have reported that the results of sulphone treatment in leprosy are much superior to those of any previous form of treatment though it has limitations. Workers in other countries are now reporting similarly. Some British and other workers have been rather critical of the new treatment but the opinion has steadily gained ground that a great step forward in leprosy treatment has been made.

Practically all this work has been done with the relatively expensive and complex proprietary sulphones promin, diasone and lately sulphetrone. Until recently no attempt was made once more because of its reputed toxicity to use the simpler and cheaper D.A.D.P.S. Cochrane (1949) reports an attempt to use D.A.D.P.S. in leprosy giving twice-weekly injections of 1·25 g. but he has found that toxic effects are too common and too serious to make this treatment widely applicable though the results were good.

Some of the criticisms made of sulphone treatment in leprosy have been shown to have little foundation. Thus the statements that it is not tolerated by many patients and that it is of value only in the severe lepromatous cases have been proved wrong (Lowe and Smith 1949). But there are two criticisms which still carry weight—that in severe lepromatous cases the treatment takes such a very long time (four years or even more) and that the treatment is too costly for wide use in poor tropical countries.

The first criticism—the length of the treatment—carries little weight because of the still greater length of hydnocarpus-oil treatment in such cases and there is also the severe discomfort of the many injections and the uncertainty of the response.

The second criticism—high cost—is the really potent one. A treatment which costs for drugs alone £10 to £15 a year per patient and may last five years is completely inapplicable on a large scale in the mostly poor tropical and sub-tropical countries where leprosy prevails. Moreover it is among the poorer sections of the population that leprosy is most common. Sulphone treatment on its present basis can never be more than a treatment for the privileged few, the vast majority of those needing the treatment must go without it.

The expense of sulphone treatment could be usefully reduced if a much more efficient and rapidly acting sulphone could be found or if the sulphones could be made much more cheaply. A sulphone which would be both cheaper and more effective would be of enormous value. This is why some leprosy workers are turning their attention to D.A.D.P.S. a non proprietary drug which can be made cheaply. The questions which this paper attempts to answer is can it be used in treating human leprosy with safety and with good therapeutic effect?

Mode of Action of Sulphones

The sulphones now in common use in leprosy—promin, diasone and sulphetrone—are derivatives of DADPS Their mode of action seems to be similar to that of the sulphonamides The question arises whether the more complex sulphones exert their antibacterial action in the form in which they are given or only when they are broken down to DADPS in the body If the latter view is correct, where does this breakdown to DADPS mainly occur—in the gut before absorption, when the drug is given by mouth, or in the body fluids or cells after absorption from the gut or, in the case of injection, from the tissues ?

Johnson (1940) studied the fate of promin after oral administration and after injection He found that, after injection, nearly all could soon be recovered in the urine as free promin in the form in which it was injected, but that after oral administration only 30 per cent appeared in the urine and some of it had undergone conjugation These findings suggest (*a*) that promin undergoes a change to DADPS in the gut before or during absorption, (*b*) that much promin given by mouth is not absorbed at all, and (*c*) that after injection very little chemical change occurs and the production of DADPS after injection must be very small

Hinshaw and Feldman (1941) found that while promin could be given intravenously in doses up to 15 g with little or no toxic effect, a dose of 1 to 3 g by mouth often produced cyanosis and other toxic effects

Because of these findings, the intravenous injection of promin became a standard method of sulphone therapy. It seems possible, however, that intravenous injection, though much reducing toxicity, reduced therapeutic activity still more

The administration of diasone has been mainly by mouth Given in this way, doses of more than 2 g a day are often toxic, as with promin Observations made here (Smith, 1949) indicate that after the oral administration of diasone, DADPS can be isolated from the urine, but most of the drug is excreted as diasone It is not clear whether the breakdown to DADPS occurs in the gut or in the body after absorption

Regarding sulphetrone more information is available Brownlee (1948) stated that when sulphetrone is given by mouth, 50 per cent or more is absorbed, practically all the drug present in the body is present as sulphetrone, and it is rapidly excreted as such, mainly in the urine The absence of acetylation and other forms of conjugation was held to imply that sulphetrone is not hydrolysed to DADPS On Brownlee's data the undoubted therapeutic activity of sulphetrone in leprosy must be attributed to the action of sulphetrone itself Findings made here (Smith, 1949) have not supported Brownlee's findings in some respects The absorption from the gut is much lower than the 50 per cent reported by Brownlee While most of the sulphone excreted in the urine is in the form of sulphetrone, a small fraction is in the form of DADPS Even before these findings were published, Brownlee (personal communication) wrote

> It appears most likely to us that it is the rate of degradation to DADPS that is important, that is to say, that the lack of toxicity of sulphetrone could quite well be consistent with a slow hydrolysis to DADPS.

In a later personal communication Brownlee stated

I have looked carefully into this matter again and can say that if sulphetrone is degraded to D.A.D.P.S. it must be degraded less than 10 per cent.

Those who have studied systematic series of sulphones such as Smith at Bethesda have concluded that the amino group or groups must be free or potentially free to have antibacterial activity. Now sulphetrone is antibacterial in the test tube and is chemotherapeutic in man. If these views are correct then the micro-organism itself must degrade sulphetrone, after it passes through the cell wall to D.A.D.P.S. We have tried to prove this point experimentally but have failed.

Thus, even according to Brownlee who appeared to be the chief exponent of the opposite view, complex sulphones possibly or probably act by being hydrolysed to D.A.D.P.S. though, with some of the complex sulphones the amount of this hydrolysis is very small.

This discussion brings us to the following important practical points. It is well established by the experience of many workers that complex sulphones given in doses producing a blood-concentration of the order of 5 mg. per 100 ml.—and often much less than this—are therapeutically active in leprosy. Most of this blood content is not degraded to D.A.D.P.S. and is therefore possibly or probably inactive. We must conclude that the minimum therapeutic blood level of D.A.D.P.S. itself in leprosy is perhaps 1 mg. per 100 ml. or even less.

The question to be investigated is whether it is possible in man to produce blood levels of D.A.D.P.S. of this order without toxic effects. The experiment outlined below was planned to answer this question.

Preliminary Trial of D.A.D.P.S. by Mouth

From October to December 1948 nine patients with leprosy were given D.A.D.P.S. daily by mouth in small and slowly increasing doses with careful clinical and laboratory examinations for signs of toxicity and the blood levels attained on different doses were estimated. The daily administration was continued for 9 weeks. The daily dose was given all at one time. The results are summarized below.

Period	Daily dose (mg.)	Resultant blood level (mg. per 100 ml.)	Toxic effects
Weeks 1 and 2	100	< 0.5	None
" 3 and 4	200	0.5–0.8	None
" 5 and 6	300	0.8–1.1	None
" 7 and 8	400	1.0–1.8	Some increase in haemolysis
Week 9	500	1.5–2.2	More haemolysis. Experiment stopped

These results were striking. The first dose of 100 mg. gave a definite blood reaction for sulphone though the blood level attained was hardly measurable. Further doses soon produced a measurable blood level and when the dose rose to 300 mg. a day the blood level averaged slightly more than the 1 mg. per 100 ml. which on the grounds outlined above, is probably a therapeutic level. Moreover, with administration once daily the

blood-level remained constant throughout the day The later stages of the experiment showed that we had a considerable margin of safety, the slight signs of toxicity at the highest dosage soon subsided when the drug was stopped

The findings showed that with 300 mg of D A D P S a day the blood-level was comparable to that attained with doses of diasone or sulphetrone five to ten times greater An explanation of this was sought, and pharmacological studies of the three sulphones were carried out here (Smith, 1949) Balance experiments to study the absorption and excretion of sulphetrone, diasone and D A D P S at different dosages, each maintained for two weeks, gave the following results at all the dosages tested

When sulphetrone was given by mouth, over 80 per cent of it was passed in the fæces and was thus apparently unabsorbed, while less than 20 per cent appeared in the urine The figures for diasone were much better, about 50 per cent being passed in the fæces and about 50 per cent in the urine For D A D P S however, the figures were much better still, less than 5 per cent being passed in the fæces and over 85 per cent in the urine Thus the absorption of D A D P S from the gut after oral administration is excellent, and this fact partly explains the blood-levels attained on such small doses But of equal if not greater importance is the slow elimination of D A D P S, mainly by the kidneys Whereas after ordinary therapeutic doses, when long treatment is stopped, sulphetrone blood-levels are not measurable after 3 to 4 days, and diasone blood-levels are not measurable after 6 to 7 days, blood-levels of D A D P S are still measurable after 14 days, and traces are found for much longer periods

Thus the low dosage of D A D P S necessary to maintain what is theoretically a therapeutic blood-level in leprosy is explained by the almost complete absorption from the gut and the slow elimination by the kidneys These facts also probably explain the toxic effects observed by Buttle (personal communication) on doses of 1 to 2 g The blood-level attained on this dosage in a few days must have been very high

Trial of D A D P S in Human Leprosy

Immediately after the preliminary experiment in the nine patients recorded above, a therapeutic trial on a considerable scale was instituted in December 1948 Fifty patients with leprosy, mostly of the severe lepromatous type, were selected Exactly the same regime was followed as in the preliminary experiment the dosage was 100 mg a day for two weeks, 200 mg a day for two weeks, and the standard dose of 300 mg a day from the fifth week onwards To begin with, frequent hæmoglobin and blood-sulphone estimations, Schlesinger's tests, liver-function tests, and other checks for possible toxicity were in force As the experiment progressed, the toxic effects were found to be minimal, and later all routine tests of this nature were abandoned as unnecessary

The number of patients treated with D.A D P S was slowly increased to nearly ninety Treatment has now (November 1949) been almost continuous for nearly a year (except for one small break of 2 weeks because of staffing difficulties) The general condition of the patients is excellent, and almost all show higher hæmoglobin values than when treatment was started (All receive 0·7 g of ferrous sulphate in a mixture freshly prepared every day) In not one single case have we seen the toxic effects—nausea, vomiting, hepatic pain, and jaundice—reported by

Cochrane (1949) after twice weekly injections of 1 25 g The experiment has thus amply proved the safety of oral administration of D A D P S by the method here outlined but as noted before the importance of slow induction of the treatment cannot be overstated The considerable safety margin is shown by the fact that in a small number of selected patients the daily dose has since been slowly increased to 400 and 500 mg a day and maintained at that level for months without toxic effects

Results in Lepromatous Cases

The lepromatous cases treated with D.A D P S for 6 months or more now (November 1949) number exactly fifty This group was a very varied and representative one including a considerable number of very severe nodular cases some with complications such as leprous affections of the eye and of the respiratory passages other cases though lepromatous were milder, with localized or diffuse lepromatous infiltration of skin and mucous membranes with few or no complications

The results on the whole have been the same as those recorded for sulphone treatment in general—slow but sure subsidence of activity of the leprous lesions gradual shrinkage of leprous nodules and infiltrations heal ing of lepromatous ulcers in skin and mucous membranes and improve ment in the patients vigour and sense of well being This clinical response to D.A D P S has certainly been no slower and has possibly or even probably been quicker than the response seen in patients treated with sulphetrone or diasone, though it is too early to make dogmatic statements on this point

Further a diminution in the number of bacilli in the lesions as shown in slit smear preparations made by standard methods is already apparent in many of our cases This is at least as great as the diminution we have seen in similar cases treated for a similar period with sulphetrone or diasone Three cases have become bacteriologically negative The results in our fifty lepromatous cases treated for 6 to 12 months, with an average duration of treatment of just over 9 months are as follows definite clinical improve ment in 36 cases (72 per cent) definite bacteriological improvement in 31 cases (62 per cent) and no cases showing clinical or bacteriological deterioration Febrile reactions (erythema nodosum) occurred in 15 cases (30 per cent) The changes in bacteriological status were as follows

BACTERIOLOGICAL STATUS

Before treatment		After treatment	
Status	Number of patients	Status	Number of patients
4+	16	4+	7
3+	10	3+	9
2+	19 (1 now neg)	2+	17
1+	5 (2 now neg)	1+	14
Neg	0	Neg.	3

The bacteriological status is determined as follows A number of microscopic slide smears are made from various sites in the body examined and graded 4+ indicates a preparation teeming with bacilli

thousands to a microscopic field 1+ represents a smear in which bacilli are few and not easy to find 3+ and 2+ are intermediate grades between 1+ and 4+ In each patient the average figure recorded in several smear preparations from different parts of the body is taken to indicate the status of the patient

In assessing the results, clinical improvement is recorded only if it is very definite and bacteriological improvement only if the reduction in bacilli is sufficient to downgrade the findings (*e g* from 4+ to 3+) Such a downgrading probably indicates on the average a reduction in the number of bacilli found in smears to about a tenth of the previous number Thus the estimates of improvement are very conservative

The period of treatment of these patients is admittedly short, at least 2 years' treatment will be needed in such lepromatous cases before a reasonably accurate assessment can be made The data so far do not justify a definite claim that D A D P S is more rapidly effective than other sulphones in lepromatous cases, though the general impressions of the staff and patients suggest that this is so

Results in 'Tuberculoid' Cases

Until recently it was stated that this milder and often self-limiting, though frequently crippling and disfiguring form of leprosy did not respond to sulphone treatment The first published report indicating that it would respond was that of De Souza Lima (1948), though his statements on the subject are cautious and a little vague Elsewhere (Lowe and Smith, 1949) we have recorded the rapid and even dramatic response of leprous lesions of this type to sulphone treatment, focal changes in the skin patches are seen within a few weeks and activity usually subsides completely within 6 months, though the inflammation of nerve trunks takes longer to subside (A fuller report is being prepared)

The accompanying table summarizes the results in fifteen such cases treated with D A D P S It will be noted that a response was seen in the lesions within a month, and sometimes within a fortnight, of treatment being started, when the dose was still 200 mg or even 100 mg a day There are here definite indications that D A D P S acts more quickly than other sulphones Moreover, activity, inflammation and thickening of the patches in the skin have tended to subside completely in a shorter time than with other sulphones In one case, in which treatment was stopped after 6 weeks because of sulphone dermatitis, the subsidence of activity of the lesions has been continuous and is now complete It is obvious that quite a short period of treatment is enough to arrest the skin lesions

In some of these patients treatment has been given for only a few months, but its effect on the thickening and inflammation of the nerves is already apparent in most cases In only three cases are nerves still abnormally tender, many still show nerves that are hard, thick and fibrotic, but in others the nerve-thickening is much less than it was In none has the neuritis been aggravated by sulphone treatment—a surprising thing considering how often painful 'reactions' in nerves arise in lepromatous cases under treatment

Thus the results of D A D P S treatment in 'tuberculoid' leprosy have highly satisfactory—at least as good as and probably better than the striking results seen with other sulphones used here

D.A.D.P.S treatment of leprosy Tuberculoid cases

Case number	Number and diameter (inches) of skin lesions	Inflammation of skin lesion	Thickening tenderness and pain in nerves	Weeks before first visible response to treatment	Weeks before complete subsidence of skin activity	Total weeks of treatment to date	Persistence of nerve lesions
	Major Tuberculoid						
1	8 (1–2)	+++	+++	3	20	40	Tenderness gone thickening less
2	12 (2–6)	+++	++	4	20	36	Nil.
3	About 50 (1–2)	+++	−	3	12	36	Nil.
4	About 20 (1–12)	+++	+	4	24	36	Some thickening slight tenderness.
5	About 24 (3–4)	+++	++	4	24	36	Some thickening no tenderness
6	12 (3–6)	+++	+	3	24	24	
7	About 20 (¼–3)	+++	+++	2	24	24	Ulnar neuritis still present
8	Over 50 (3–6)	+++	+	2	12	28	Some thickening no tenderness.
9	About 50 (¼–3)	+++	+	4	16	20	Nil
10	About 10 (¼–2)	+++	+++	2	20	20	Thickening less no tenderness.
11	Over 50 (1–3)	+++	++	4	Still incomplete	10	" "
	Intermediate Tuberculoid						
12	Several hundred (small)	++	+	3	12	36	*Nil*
13	Innumerable (small)	++	+++	3	24	32	Thickening and tenderness almost gone
	Minor Tuberculoid						
14	Several hundred (small)	+	−	3	12	36	Nil
15	3 (¼–3)	+	−	3	24	24	Nil

Practical Aspects of D A D P S Treatment

Difficulties

The difficulties encountered in establishing and maintaining D A D P S treatment are not serious, they are of the same kind as are experienced with more complex sulphones, though probably milder

The incidence of *febrile reactions* (erythema nodosum) in lepromatous cases has been 30 per cent, this is almost exactly the same incidence as with sulphetrone, and the severity and duration of these manifestations has been no greater than with sulphetrone We suspend sulphone treatment until the condition has subsided

Anæmia has been no more and probably less, common or severe than with sulphetrone, a possible factor here is that sulphetrone forms an insoluble compound with iron in the gut (Brownlee, 1948) and may thus prevent iron absorption When D A D P S, with its much smaller dose is used, this factor may be absent or less active

Leprous *neuritis* and leprous *eye inflammation* may be precipitated by D A D P S in lepromatous cases, just as by the other sulphones, but they are no more common or severe Once again we suspend treatment until acute symptoms have subsided

A drug *dermatitis,* which may progress to exfoliation, may occur with D A D P S, as with other sulphones, between the 3rd and 5th weeks of treatment Among nearly ninety patients treated with D A D P S we have had three such cases, two however occurred among six patients in whom, as an experiment, the dose had been increased at twice the usual rate Only one case of dermatitis has been seen in over eighty cases treated under our normal regime The dermatitis subsides on the cessation of treatment and the oral administration of anti-histamine drugs, we have used 'Anthisan' In these cases, sulphone treatment must be withheld for at least 2 months, and often it can be resumed only after the patient has been desensitized with repeated small and increasing doses, these are best given by injection, working up from 2 mg or even lower levels, if necessary In sensitized patients, dermatitis may appear within a few hours of administration, so daily injections are recommended for desensitization

Intercurrent *bacterial infections* during sulphone therapy are not common, but when they do occur they are unlikely to respond to sulphonamides This is probably because the ranges of activity of sulphones and of sulphonamides overlap widely, organisms resistant to sulphones are likely to be sulphonamide-resistant For this reason penicillin plays an important part in the treatment of intercurrent disease in sulphone-treated patients Here the commonest conditions requiring penicillin therapy are pneumonia and 'tropical' myositis In patients under sulphone therapy the ordinary septic complications of leprosy rarely arise, presumably because of the wide range of activity of the sulphones

Cost

The price of 100 mg tablets of D A D P S is 14*s* a thousand A patient treated by the method here outlined will require on the average thousand tablets a year, so the cost will be 14*s* a year for drugs The st of treating one patient with diasone or sulphetrone is at present

£10 to £15 a year Thus the use of D A.D P S has reduced the cost of sulphone treatment to about a twentieth of the previous figure

In Nigeria treatment with hydnocarpus oil is now no cheaper than with D.A D P S, and in addition to the oil there is the big expense in syringes needles, sterilization, and staff to give the injections Moreover the results are greatly inferior

Financial considerations now prevent the wide use of the complex proprietary sulphones, but with D A D P S it should be possible to treat all the thousands of cases of active leprosy in the Nigerian leprosy institutions In other countries the same factors will operate in varying degrees

Possible Modifications

Our present regime is based on a standard dose of 300 mg given once a day The question arises whether daily doses are necessary A small group of cases is being treated with twice weekly doses given by mouth the regime being 1st week 100 mg doses, 2nd week 200 mg doses, and so on to 500 mg doses in the 5th week this dose being then maintained The blood levels range from 2 mg per 100 ml soon after the dose to 0 3 mg just before the next dose. Toxic effects are not serious and clinical improvement is beginning to appear Injections seem quite unnecessary for twice-weekly treatment Such a regime would be suitable for outpatients and would reduce the cost of treatment to 7*s* a year

A further question is whether on daily administration, a dose of 300 mg a day is necessary or advisable This will be investigated later We already know that, in tuberculoid cases daily doses of 100 mg are therapeutically active but in these patients bacilli are very few and natural resistance is high It would therefore be wrong to argue that 100 mg a day is sufficient for heavily infected lepromatous cases with no natural resistance Nevertheless there are indications that improvement is not proportional to the size of the dose Our patients on 400 and 500 mg a day are not so far showing an appreciably more rapid improvement than those on lower doses but the period of treatment is too short for a sound judgment. The best standard dose may turn out to be less than our present 300 mg and if so the cost of treatment will be still further reduced

Requisites

The main and in fact the only real necessity for D A.D P S treatment is the supervision of a sound clinician who knows his leprosy Proper clinical examination before and during treatment and the regulation of treatment according to the findings are all that is really needed During the first few weeks of treatment a weekly examination is advisable later an examination fortnightly monthly or even less frequently may suffice provided the patient can refer to the physician at once if need arises A few beds for temporary admissions during 'reactions are very useful

The giving of the proper doses must be adequately supervised Primitive people often think that they cannot have too much of a good thing A big dose of D.A D P S particularly in the early phases of treatment may be dangerous. Moreover a patient may be tempted to keep and sell some of his tablets instead of swallowing them

Laboratory facilities can be very simple To judge the results of treatment accurately microscopical examination of smears is of course necessary Hæmoglobin estimations are useful but the good physician will

detect anæmia clinically The Schlesinger's test for urobilin in the urine is useful in cases of suspected toxicity, for the test with Ehrlich's reagent does not work when sulphones are present in the urine The results must be interpreted with care, for disordered liver function and a positive Schlesinger's test are common in 'normal' Africans Blood-sulphone estimations are unnecessary as a routine measure, though they can easily be done with the Lovibond comparator and they add to the value and interest of the work from the physician's standpoint

Discussion

The introduction of the sulphone treatment by workers in the U S A began a revolution in the treatment of leprosy, whose magnitude is only now becoming apparent and is little realized in the United Kingdom, where publications have been few and opinion has been divided, for while Muir (1947, 1948) and Davey (1948) have written enthusiastically of the treatment, Cochrane (1947), Rogers (1948) and *The Lancet* (1948) have been more critical Cochrane, in later publications in specialist journals (1948, 1949), has shown increasing interest in an enthusiasm for sulphone treatment, his latest report being on 54 treated lepromatous cases, all of which have improved, some markedly, ten of them becoming bacteriologically negative

The number of sulphone-treated cases reported on by British workers has been small, usually less than fifty, and the period of treatment has usually been only a few months, though the 54 cases reported by Cochrane (1949) have been treated for 2½ years Here at Uzuakoli, Nigeria, the number of cases treated (first by Davey and later by Lowe) has been over 350, and the period of treatment has been up to nearly 4 years, the evidence of the great value of the treatment has been overwhelming (Lowe and Smith, 1949)

In 20 years' experience of treatment with hydnocarpus oil and its derivatives, with a growing appreciation of the frequently self-limiting nature of leprosy, I gradually became more and more sceptical of the specific value of this treatment It often produces clinical improvement in the milder cases, particularly tuberculoid cases, and it accelerates the strong tendency to spontaneous arrest In mild lepromatous cases it sometimes produces apparent arrest of the disease, but its action is very uncertain, and relapse is common In lepromatous cases in general, particularly the severer ones, the ability of hydnocarpus oil to modify the course of the disease is often very limited Years of painful treatment often accomplishes little The argument advanced by some that hydnocarpus treatment is of value because it prevents the tuberculoid cases from becoming lepromatous is negatived by the finding that even without treatment this change is very rare

The change in outlook produced by sulphone treatment is one of the most striking achievements of modern medicine The full action of sulphone treatment in severe cases is very slow but amazingly certain The physician can now feel absolute confidence that an active case of leprosy, no matter how severe, will respond to sulphone treatment, that the disease will cease to progress from the time when the treatment is begun, and that the lesions already present will slowly subside and the infection gradually die out

The use of D.A D P S has certainly overcome the difficulty of the cost of sulphone treatment Whether its use will reduce the duration of treatment remains to be seen It has at any rate made sulphone treatment possible for a vast number of patients in tropical countries whereas previous forms of sulphone treatment could not be more than the privilege of the few

The question arises whether the findings here recorded may not have an important bearing on the sulphone treatment of tuberculosis So far in human beings this has been rather disappointing Only the complex sulphones have been used Since D.A D P S appears to be the most active of the sulphones and can be safely used in man it may be of value in human tuberculosis Its value in experimental tuberculosis has already been demonstrated but its reputed toxicity has prevented its use in the human disease A few preliminary observations made here have shown that D.A D P S treatment as here outlined is well tolerated by patients with tuberculosis of the lungs and a proper trial is well worthy of consideration

Summary and conclusions

The special properties of D.A D P S are outlined *In vitro* and in animals its antibacterial power is possibly the greatest of any of the sulphones

The accepted idea that D A D P S is too toxic for use in human beings is examined and found to be erroneous

A regime of oral administration of small doses rising very slowly from 100 mg a day to the standard 300 mg a day in 5 weeks is recommended treatment being continuous This regime does not produce toxic effects of any consequence and it will maintain a blood level of about 1 mg per 100 ml which on theoretical grounds should be a therapeutic level in leprosy

The almost complete absorption from the gut and slow elimination by the kidney explain the relatively high blood levels attained with such small doses and also explain the toxic effects reported with the much higher doses used by others

In the avoidance of toxic effects very slow induction of D.A D P S treatment is of paramount importance

A therapeutic trial of this treatment in 88 patients with leprosy for periods up to a year is described

Of the fifty lepromatous cases treated for more than 6 months none show deterioration 72 per cent show clinical improvement 62 per cent show bacteriological improvement and three have become bacteriologically negative. These results compare very favourably with those seen here with complex proprietary sulphones There are indications that D A D P S is acting more rapidly than these other sulphones

In fifteen tuberculoid cases treated for 4 to 10 months the response has been apparent within a month and sometimes within a fortnight or less with complete subsidence of activity of the skin lesions within 6 months the nerve involvement however takes longer to subside The results though similar to appear to be more rapid than those seen with other sulphones in similar cases

The cost of D A D P S for the treatment of one patient for a year on this basis is 14*s* The cost of treatment with the complex proprietary sulphones is about twenty times as much

A regime for twice-weekly administration of D A D P S by mouth suitable for outpatients is outlined, the cost being 7*s* a year per patient Injections seem to be unnecessary

It is suggested that the more complex sulphones act by being hydrolysed to D A D P S in the body They are incompletely absorbed from the gut and incompletely hydrolysed to D.A D P S , they thus provide an unnecessarily elaborate and expensive method of securing the action of D A D P S in the body Administration by injection, by preventing hydrolysis in the gut, may even reduce their therapeutic activity

The administration of D A D P S itself by mouth is safe, simple, and very cheap It seems to be the most rational form of sulphone treatment

Reconsideration of the sulphone treatment of human tuberculosis may be advisable in the light of the findings recorded here Preliminary observations show that D A D P S treatment as here outlined is well tolerated by patients with tuberculosis of the lungs

Addendum—Since this paper was written, the treatment has been continued without a break In the original 50 lepromatous cases, the average period of treatment is now (January 1950) 11½ months, clinical and bacteriological evidence of improvement is correspondingly stronger—78 per cent now show a reduction in the figure for bacteriological status, and 3 more cases (all originally 1+) have become negative The bacteriological status of the 50 cases is now as follows 4+, 2, 3+, 7, 2+, 13, 1+, 22, negative, 6

Studies carried out in Nigeria show that a lower dosage is effective, and similar findings have been made elsewhere (Molesworth, 1949 and Muir, personal communication) It is found here that a weekly dosage of 700 mg (1 tablet of 100 mg a day) is usually enough to produce a good clinical and bacteriological response, but a dose higher than this is preferred At present patients are being treated on four different dosage systems —

1	300 mg for six days a week	weekly dosage 1 8 gm
2	300 mg alternate days excluding Sundays	weekly dosage 0 9 gm
3	200 mg six days a week	weekly dosage 1 2 gm
4	500 mg twice a week	weekly dosage 1 0 gm

There is so far no significant difference in the response to these different dosages in lepromatous cases, but in the tuberculoid cases, daily administration appears to produce a more rapid response

The lower dosage is somewhat more easily tolerated, though little serious trouble has been encountered on the higher dosage Since these studies were undertaken three different workers in different parts of India have written personally to the author saying that Indians appear to tolerate D A D P S less readily than Africans, and that the dosage originally recommended by the author (300 mg a day for seven days a week) is too high for them, a progressive anæmia is not uncommon The author assures those workers, experiencing the difficulty, that the dosage of D A D P S can be considerably reduced with little or no loss of therapeutic efficacy

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ABSTRACTS FROM CURRENT LITERATURE

International Journal of Leprosy, Vol 17, No 4, October-December, 1949

Comparative Studies of the Cardiolipin Antigens with the Regular Antigens in the Kolmer Complement Fixation and the Kahn Precipitation Tests in Leprosy By H Ross and F Gemar

Cardiolipin is a phospholipin isolated from the beef heart muscles by Pangborn According to Giordano cardiolipin antigens give results of maximum sensitivity and of much greater specificity in tests for syphilitic reagin than do the antigens commonly used Kline believes that, because of their superior quality, the cardiolipin-lecithin-cholesterol antigens should soon replace those now used in tests for syphilis A comparative analysis of 3 serological reactions in 225 cases of leprosy, predominantly of lepromatous type, and free from syphilis as far as was known, showed the following results Kolmer positive 169, doubtful 23, negative 33, Kahn positive 214, doubtful nil, negative 11, Mazzini (slide flocculation) positive 111, doubtful 36, negative 78

The present study included Kolmer and Kahn's tests, using both regular and cardiolipin antigens side by side, of 225 cases, mostly of lepromatous type Of these cases 101 were found to be positive and 54 negative with all four of the antigens Among the remaining 70 cases there was more or less discrepancy It was apparent that fewer positive results were obtained with the Kahn cardiolipin antigens than with his regular one, the latter gave 159 positive against 112 with the former In the Kolmer tests the reserve was found, namely 151 positive with cardiolipin antigen, and 101 with regular one The lesser number of positive Kolmer and Kahn reactions in the present work as compared to previous work on the same patients is regarded as a result of the intensive sulphone (promin and diasone) treatment of the patients

Leprosy in Fiji and South Seas By C J Austin

The advent of leprosy in Fiji have been much earlier than 1837 when Lyth recorded treatment of such cases by him

The Government of Fiji established a leprosy settlement on the island of Beqa fifty years ago This was abandoned in 1911, when the Makogai settlement was opened The number of inmates in the settlement is at present (1948) 669 of which 429 were from Fiji and 240 from other regions The number of known cases of leprosy is very little short of the true number and the number of missed cases is minimal

In total 3,032 patients have been admitted into Makogai since 1911, including 2,417 from Fiji itself and 615 from beyond the colony Adding the 429 Fijian patients still at Makogai to the 388 discharged patients still alive and being reported on, the total of 817 cases of leprosy—active and inactive—gives an incidence for Fiji of about 3 per 1,000 At present Fiji is spending £45,000 per annum on the leprosy work and is recovering approximately £18,000 from other administrations

Leprosy in Niue Island A Note on the History of the Disease By G O L Dempster

Niue is a coral island approximately 10 miles in diameter and 64 000 acres in extent It is one of the Pacific group of islands in Oceania. The inhabitants are people of the Polynesian stock and numbered about 4 104 in 1936 Leprosy has been introduced in the island not later than eighties of the last century There has been up to the end of 1938 a total of only 19 leprous persons 9 males and 10 females over approximately the last fifty years Leprosy has never become widespread in this island, as in other Pacific islands The disease remained localized to two families.

The Pharmacologic and Chemotherapeutic Action of some new Sulphones and Streptomycin in Experimental Tuberculosis By M I Smith E L Jackson J M Junge and B K Bhattacharya

The authors summarize and conclude their article as under

A comparative study is presented of the pharmacologic and chemotherapeutic properties of (1) 4 4'-diaminodiphenylsulphone (DDS), (2) promin (3) sulphetrone, and (4) 4 amino-4'-β-hydroxyethylaminodiphenylsulphone (hydroxyethyl)

The intravenous toxicities of promin and sulphetrone in rats are almost identical if computed on the basis of DDS equivalent

The oral toxicities of sulphetrone and hydroxyethyl are much less than that of promin. The low toxicity of sulphetrone appears to be due to poor absorbability

The blood levels following oral administration of hydroxyethyl are relatively low This is not due to poor absorbability but rather to a preferential localization of the compound in certain organs and tissues of the body *e g* liver kidney lungs and spleen. About 50 per cent of the dose administered is excreted in the urine in 24 hours and undetermined but appreciable amount possibly 25 per cent is eliminated in the bile

There is evidence to indicate that promin and sulphetrone are metabolized in the body to the parent substance DDS There is evidence that hydroxyethyl is not metabolized to DDS

Hydroxyethyl has a good chemotherapeutic activity in experimental pneumococcus infection *in mice Its activity in experimental tuberculosis* in guinea pigs compares favourably with promin Like promin it potentiates the action of streptomycin Sulphetrone has a lower activity when used alone and when used with 5 mg per kg per day of streptomycin the effect was additive When used with the large dose of 25 mg per kg per day of streptomycin some potentiation of action was obtained'

Silvering of Lepra Bacilli in Tissues By F L Blanco and G L Fite

The authors' summary and conclusion is reproduced below

Lepra bacilli are readily silvered in blocks of lepromatous tissues with Jahnel's and other methods

Bacilli silvered in the block undergo a minimum of distortion and yield a true picture of the infection of the tissues scarcely obtainable with

other methods While such silvering is not practical as a routine clinical-pathologic procedure, it is highly valuable in the study of the lepromatous lesion

Study of silvered sections shows that past concepts of the morphologic aspects and arrangements of bacilli are open to considerable revision Actively growing organisms resemble minute colonies of fungi, and do not appear as "bundles" or "cigar packs" A new concept of the nature of the globus is offered

Different degrees of silvering observed indicate that the weakly silvered bacillus constitutes one form of the degenerating organism'

Leprosy Review, Vol XXI, Nos 1 and 2, January–April 1950

The Fate of Injected 4 4'-*Diammo-diphenyl-sulphone in Humans and Guinea-pigs* By I A Simpson and B D Molesworth

The authors' summary is reproduced below

'(*i*) Extracts of tissue and of urine from cases that have received injections of 4 4'-diamino-diphenyl-sulphone have been found to develop a colour, when diazotized and coupled with N-(1-naphthyl)-ethylene diamine, which differs slightly from the colour developed by solutions of pure 4 4'-diamino-diphenyl-sulphone

(*ii*) Absorption curves of the coloured solution obtained from these extracts and solutions show that the former possess maximum absorption at $\gamma = 545$ millimicrons while the latter show maximum absorption at $\gamma = 550$ millimicrons

(*iii*) The possible existence in the body of a labile conjugated form of the sulphone is suggested

(*iv*) A few 4 4'-diamino-diphenyl-sulphone tissue levels as found in guinea-pig tissues and human tissues are recorded'

The results obtained in the cases of guinea-pig tissues show that the highest sulphone levels are found in the kidney and liver (3 2 mg and 3 4 mg per 100 gm. of tissue respectively) They are low in the brain tissue A certain degree of the localization of the drug appears to occur in the skin and muscle tissues near the site of subcutaneous injections in oil

A Pharmacological Study of Three Sulphones Part III The Specific Toxic Phenomena By M Smith

The study of the toxic effects of the sulphones commenced in Part II of the report has been continued Endeavour has been made by the author to discover how far direct toxic hæmolysis is responsible for the anæmia The evidence for the hæmolytic process was clear cut only in the case of diamino-diphenyl-sulphone It is concluded that the anæmia produced by sulphones is not a simple process of hæmolysis, but is probably mainly dyshæmopoietic in nature

Twenty-six cases under continuous sulphone therapy for 2½ years showed no evidence of disturbed liver function

Diamino-diphenyl sulphone (in oral doses not exceeding 0·1 gm daily) is suggested as a therapeutic agent for the treatment of leprosy for the following reasons

(*i*) it is extremely well absorbed

(*ii*) it is slowly excreted

(*iii*) in the dosage suggested it is no more toxic than the proprietary sulphones

(*iv*) the cost of therapy with diamino diphenyl sulphone is less than 1/10th of that with the proprietary sulphones

In cases of known kidney dysfunction the oral dose of diamino diphenyl sulphone should not exceed 0·1 gm daily

The oral administration of sulphetrone should be replaced by parenteral administration owing to the poor absorption of this drug A suggested dosage is 3·0 gm weekly given in two 10 ml injections of a 25 per cent aqueous solution

Sulphetrone would seem to be a completely non-toxic substance If its anaemia producing effect is excepted in the dosage recommended for leprosy therapy

The anaemia produced when the proprietary sulphones are administered parenterally is much less than that produced when oral administration is used

The sulphones cannot be shown to have any effect upon the renal function

No effect upon the white blood count or picture can be demonstrated

It is suggested that the estimation of blood levels of the sulphones as a means of adjusting dosage is an unnecessary procedure

Further clinical study of the effect of various dosage regimens of the sulphones is strongly advocated'

Some Experiments with Injected Sulphetrone By A L Relwicz

Investigation was undertaken by the author with sulphetrone to see whether appropriate blood-level could be maintained by means of injection 13 patients (9 males and 4 females) were given subcutaneous injections, in the arm or thigh All the patients were adults the average weight of each was 131 lbs

It was found that four hours after injection of 7 cc of a 20 per cent aqueous solution the average level of sulphetrone was 5 5 mg per cent which seemed to be rather low for effective treatment With an injection of 10 cc of the same, there was no significant rise in the level either after four hours or on the following day In both cases after 72 hours nearly all sulphetrone had been eliminated from the circulation

When 5 cc of a 33 per cent aqueous solution was injected subcutaneously, the blood-level was on an average 9 mg per cent after 1 hour, 10 mg per cent after 4 hours, 3 5 mg per cent after 24 hours, about 2 mg per cent after 48 hours and a trace after 72 hours No toxic effects were seen with this higher concentration So it seemed on economic grounds, that it was necessary to administer the drug by the latter method the injections being given at least on alternate days The blood-level of sulphetrone given by injection on alternate days as above, had not risen to toxic level after 15 days

A Case of Filarial Elephantiasis of the Face resembling Nodular Leprosy By J Barnes

The patient, an elderly male African, presented bulbous masses over nose and infraorbital region Lips were enormously thickened The rest of the face was thickly infiltrated and a toe was missing The total duration of the disease was 15 years All the cardinal signs of leprosy were absent Microfilariae were found in the wet blood smears taken from the nodules

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Public Health Reports, Vol 65 No 7, February 17 1950 pp 195–207

Promacetin in the Treatment of Leprosy By F A Johansen *et al*

Promacetin (Parke, Davis & Co) is sodium 4, 4' diammo-diphenyl-sulphone-2-acetyl sulphonamide It is a white crystalline compound soluble up to 3 per cent in water at room temperature It gives a protection against tuberculosis in guinea-pigs

The clinical material for this preliminary evaluation of promacetin included 27 patients—26 of the lepromatous and 1 of the tuberculoid type Most of the patients were either moderately or far advanced with unfavourable prognosis

The initial daily oral dose of promacetin varied from 0 3 to 0 5 gm and was increased by 0 3 to 0 5 gm every two weeks until a total daily

dose of 1 5 gm was reached Then the dose was increased by either 1 0 gm or 1 5 gm. up to a maximum of from 3 0 to 4 0 gm daily Promacetin was administered at meal time and rest period for 15 days was observed at intervals of a few months The period of observation in this study covered 17 months

Among this group of 27 patients there occurred no severe acute toxic symptoms

Slight depression of erythrocyte counts was noted in 14 patients in the first 2 to 4 weeks of treatment Seven of these patients who did not receive any anti anaemia treatment returned as rapidly to their original level of erythrocytes as those who were given such therapy

Twenty-one patients, who had clinically active lesions (including the tuberculoid case) were treated for periods varying from 4 to 16 months and the total amount of the drug administered to each patient averaged 658 gm

The condition of the skin improved markedly in 9 moderately in 5 slightly in 6 and 1 only became worse Number of bacilli in skin smears decreased in 9 (including one in which the smears became negative) remained the same in 10 (including the tuberculoid case which was negative all through) and became worse in 2 Nasal smears improved in 15 cases of which 10 became negative from highly positive ones

Six patients presented only residual lesions and were treated for periods varying from 3 to 15 months Each patient received 435 gm of promacetin on an average Four of these patients began to show renewed clearing of their skin after 3 to 6 months treatment There was a reduction in the number of leprosy bacilli in the skin of the 4 patients who showed renewed clearing of the skin and one became negative While two had positive nasal smears at the inception of treatment all of the 6 had negative nasal smears at the end of that treatment interval

It was found in the determination of promacetin blood levels that the blood level remained fairly constant between 1 5 and 2 0 mg per 100 cc of blood on oral doses varying from 3 0 to 4 0 gm daily irrespective of the length of treatment After 9 months of treatment some patients excreted by way of the kidneys almost as much of the drug daily as was administered. After prolonged treatment significant amounts of promacetin were excreted in the urine up to 12 days following discontinuation of the drug

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Journal of Pathology and Bacteriology, Vol 60 pp 93–122 1948

A New Mycobacterial Infection of Man

I *Clinical Aspects* By P MacCallum

In 6 cases of ulceration of the skin occurring in Australia a mycobacterium hitherto unrecorded was found in the lesions Ulcers were single in 4 instances located between knee and ankle and in 2 on forearm Three were male and 3 female patients their ages varying from 2½ to 51 years There was no definite evidence of tuberculosis or syphilis

Acid-fast bacilli were found in sections, but there was no sign of tubercule follicles, giant cells, endotheloid grouping or caseation in any of these sections

II *Experimental Investigations in Laboratory Animals* By J C Tolhurst *et al*

Ascites developed after an interval of about 8 months in 49 of 52 male rats inoculated intraperitoneally with material from 3 patients 1 to 2 months later, œdema and ulceration of feet and tail occurred Acid-fast bacilli were found both in the ascitic fluid and ulcers

III *Pathology of the Experimental Lesions in the Rats* By H A Sissons

The outstanding feature after intraperitoneal injection was establishment of gross lesions on the peritoneal surface of scrotum and contents, with massive peritoneal effusion No macrophage, vacuolated or foamy, was seen The bacilli from rat-lesions resemble morphologically that of human tuberculosis Collections frequently occupy mononuclear and occasionally polymorphonuclear phagocytic cells in ascitic fluid Bacillus is gram-positive if methyl-violet stain is warmed, and strongly acid-fast

IV *Cultivation of the New Mycobacterium* By G Buckle *et al*

The organisms grow well in yolk agar or Petragnani media, at 30°C Growth was slower and scantier than that of human tubercule bacillus Colonies were lemon to mustard yellow in colour on Petragnani's medium after 4 weeks Low concentration of glycerine enhanced growth Cultures obtained from peritoneal fluids of inoculated rats produced the disease in other rats Morphologically the bacilli from cultures were rod-shaped, slightly curved and strongly acid-fast Dr Wade has suggested the name mycobacterium ulcerans for their newly discovered bacillus

REPORTS

Premananda Leper Dispensaries, Annual Report for 1949

The dispensaries are two in number one situated in the southern part and the other at the northern part of Calcutta Dr D P Dutta is the Chairman of the Managing Committee and the Revd Father P Thornan the Honorary Secretary and Treasurer

The total number of cases treated at the two clinics including the beggar patients was 4 643 Of these 1 615 were new' cases, 2 528 were old cases and 500 beggar patients Of the total cases other than the beggar patients 3 406 were male and 737 female 3,203 came from inside the city and 940 from outside 1,220 were infectious and 2,923 non infectious 2 337 cases attending regularly for treatment were re examined at the end of the year with the following results —Disease arrested—138 much improved—863 slightly improved—1 019 stationary—317

As a result of 217 home visits only 27 of absentee patients were persuaded to attend again Treatment consisted mainly of giving 'Hydnocarpus oil' injections The total income for the year was Rs 24,664| and the total expenditure Rs 21 064|

Victoria Leprosy Hospital, Dichpali, Hyderabad State, India, Annual Report for 1949

The usual activities in the hospital were carried on viz teaching, gardening farming recreation of patients etc A limited number of highly infective cases were treated with diasone and sulphetrone A new research department has been opened during the year Massage radiant heat exercises splinting etc., were successfully carried out in the physiotherapy department The annual course in leprosy was held for the students of the Osmania University

During the year 211 new admissions were made 286 were discharged (of which 210 were made non infectious) 4 patients died the total number of patients at the end of December 1949 being 572 The number of patients admitted to medical wards for lepra reaction dysentery etc was 420 Patients admitted to surgical wards for ulcers amputation etc, numbered 126 out patients coming from nearby villages numbered 180 temporary admissions in the ward from outside institutions for medical and surgical conditions were 256

Sixty thousand lbs. of fruits and vegetables were supplied from farm and garden of which tomatoes were 15 000 lbs and onions 7 000 lbs The yield of rice was 30 000 lbs

One hundred and twenty four patients (the largest number) were admitted into the hospital from the Gulberga district of the State the lowest

number of 5 being from Bheed The total grant from the district local fund amounted to Rs 12,148|-, the largest sum of Rs 2,036|- coming from the Aurangabad district fund

The local contributions amounted to Rs 1,256|- The total receipts amounted to Rs 1,15,282|-, the largest contribution of Rs 42,197|- coming from the Nizam's Government The total expenditure amounted to Rs 1,54,491|-, a sum of about Rs 52,000|- being spent on food and salaries each

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British Empire Leprosy Relief Association (Madras City Branch), Annual Report for 1949

The city branch continued its usual activities, and in the report is included the work done by the Association during the past 17 years The funds of the Association consist mostly of money raised from Flag Day, together with contributions from the Madras Race Club and Corporation With increased grant from the Corporation, it is proposed to appoint a Welfare and Propaganda Officer by the Association In the bi-weekly clinic in Choolai over 3,000 injections are given annually The average attendance is about 40 on each treatment day The Choolai clinic building is proposed to be improved Another activity of the Association is the treatment of children at special clinics, most of whom are from the corporation schools Some endemic areas have also been selected for the follow-up of children affected with leprosy The work in Washermenpet Investigation Centre and Leprosy Unit is chiefly one of follow-up of registered cases, detection of new cases and propaganda This work has been extended to 7 other areas

The report next deals with the leprosy investigations carried out so far in the Madras City—its population, number of children, density of population and housing condition, facilities for indoor and outdoor treatment, examination, treatment and follow-up of school children, and survey of 3 different parts of the city

In 1934 the Madras Leprosy Council, now known as the Madras City Branch of B E L R A, opened a clinic in Choolai and another in Triplicane With special donations collected by this Leprosy Council, six blocks were constructed in the Lady Willingdon Leprosy Sanatorium, Chingleput, for the benefit of cases from the city In 1940 an intensive survey of Washermenpet was done, and two afternoon clinics were opened in that area A survey of all the schools in the Vepery and Purusawalkam was completed In 1945 examination of all non-corporation schools in the city was commenced, but in 1947 when the re-examination was half-completed, it had to be stopped Another weekly leprosy clinic for corporation school children was opened in Kasturba Hospital, Triplicane A skin and leprosy clinic for women and children was opened in the same hospital, but had to be closed later on Special clinics for children are held in the two B E L R.A centres, and in 1947-48, 251 children attended and were treated Of these 239 were definite cases and 12 suspicious cases, 94 were below 10 years and 157 above 10 years The results are given of the investigation in school children, follow-up of children suffering from leprosy, and survey of 3 different parts of the city carried out so far

The report then mentions certain general observations in regards the following —(1) marital life and leprosy (2) fecundity of female patient, (3) conjugal infection (4) childhood infection (5) communities affected (6) immigration industrialization and altitude in relation to leprosy, (7) attitude of the public medical men and school authorities towards leprosy and (8) legislation

Regarding the approximate incidence of leprosy in Madras City it is said that the disease is not evenly distributed throughout the city The incidence among all children is not likely to exceed 1 per cent Estimated on the total child population of 4½ lakhs, the number of children suffering from the disease will not exceed 4 500 of which half belong to the benign type It can be said that there are not more than 15,000 cases of leprosy in the city The percentage of infectious cases to the total number of cases is about 13 per cent The number of infectious cases in adults is about 2 000 The total number of infectious cases in the city including adults and children will be about 5 000 and this constituted the chief problem of control

Leprosy field investigations done in Saidapet, by a special investigation staff for over 10 years (which now forms part of the city), are included in the report

The report then outlines certain suggestions for the control of the disease in the city This is followed by six tables showing the statistics of survey undertaken in the different areas and a map of Madras City showing the incidence of leprosy

The total income of the city branch for the period amounted to Rs 3,872| and the total expenditure Rs 4 170| leaving an asset of Rs 20 078| in hand

LEPROSY IN INDIA

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(Ed—Editorial, OA—Original article, RA—Reprinted article, R—Report, CR—Clinical report, C—Correspondence)